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The Bancroft Memorial Lecture.[1]

THE LAW OF LIFE.

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Melbourne.

Curiosity is one of the most permanent and certain characteristics of a vigorous intellect.

SAMUEL JOHNSON, *The Rambler*, Number 103.

YOUR COUNCIL has done me the honour of inviting me to present the twenty-fifth Bancroft Oration. After the orations are reviewed of prominent Australian anatomists, physiologists, parasitologists and clinicians of a quarter of a century, there seems little new left to be said about the pioneer in whose memory this lecture is given. Indeed, I will not attempt any discussion of Joseph Bancroft himself, though I can say with several of my predecessors that his contribution to pathology and medicine was one of the prominent and best remembered landmarks of my student days. This kind of contribution—the observation made with very few facilities—has a deservedly great influence on us. It emphasizes so well that curiosity which is the characteristic of the vigorous intellect.

This beacon, lit by the hand of a busy practitioner, constitutes a guide, therefore, for any who might wish to sail the difficult seas of original investigation. It shows that information is to be obtained by the intelligent and persistent investigator in what are, by modern standards which demand palatial laboratories, the most unlikely circumstances. Indeed it makes clear that much is to be gained by simple observation of the experimental animal—in this case the patient—without recourse to other than clinical examination and the simple observation of clinical and pathological material.

I propose to discuss with you this evening a group of conditions, the elucidation of which is greatly assisted by such observation. It goes without saying that all methods of observation have their own importance. It has been said that "life is like a library owned by an author; in it are a few books which he wrote himself, but most of them were written for him". We can and do take an interest in the contributions of others, but it is important that we continue to make our own.

One significant point about a library is that ideas become fixed because they are actually printed. This has been pointed out by Lancelot Hogben ("Cave Painting to Comic Strip", 1949) when he shows that the spelling of some words is fixed more or less at that of the sixteenth century, though pronunciation, which originally determined the spelling, has changed. Similarly, ideas become fixed. It is all the more important then that, independently of other sources of knowledge, we should continue individually to accumulate information and by applying it thus prevent ideas from becoming rigid. Amongst the many kinds of observations that have been employed, the simple clinical one plays a most important role.

Various special kinds of inquiry provide the basis for much that is to be seen in the literature, but too much attention must not be attached to any one of these. It is necessary all the time to make our own studies and to assess critically, in the light of our own, those made by other means. Thus, though we give due prominence to conclusions drawn from observations of special kinds, we should not allow our own to be submerged by them.

In the conditions that we are to discuss, quite definite views as to their nature have been developed and are stated in the literature, but I propose to show that simple clinical and pathological study, if we only observe suf-

[1] Delivered at a meeting of the Queensland Branch of the British Medical Association on August 4, 1950.

ficiently carefully, will demonstrate, or at least indicate, the error of some of them. Our mistakes are due to our deceiving ourselves[1] by ignoring information which is at our hand, not because we have any good reason for being led astray.

So, in the spirit which would quite certainly have imbued Bancroft, we may now examine some of these conditions. At first sight these may appear to be a somewhat heterogeneous group, but it will be shown that they have definite points in common. In dealing with them it is necessary to consider the common generally accepted views as to their origin and nature, and from this we may proceed to a consideration of such features as are not in conformity with these opinions.

Telangiectases.

Telangiectases are small localized dilatations of peripheral blood vessels occurring in the skin, mucous membranes or other organs. They are recognized readily, of course, in the living person in the former situations. Incidentally, as might be expected, they are not easy to recognize after death since they are demonstrable only when the vessels are distended with blood. Each little group of vessels is supplied by an arteriole, and they occur singly, sporadically or scattered widely over the body.

The best-known form is one which has been observed to occur in families and is regarded as hereditary in origin —due to some genetic peculiarity of the blood vessels. Another variety is the sporadic one, which does not usually have as wide a distribution on the body as the former. By analogy with the former, however, this is often considered to be related and due also to some hereditary peculiarity.

A number of observations made over many years, but emphasized in the last two decades, demand some attention.

1. Vascular dilatations are observed to come and go. In a particular area there may be approximately the same number at one time as there was at another, but if they are observed carefully it will be seen that whilst one actual area of dilatation becomes normal, that is to say the dilated vessels resume a normal calibre, in an adjacent zone another vessel group becomes dilated. This, of course, would suggest that the condition is not due to some disturbance or peculiarity of a specific vessel; it is due rather to some factor acting variably over an area of tissue.

2. The vascular changes occur in relation to some special conditions—that is, they do not constitute a disease *per se*. First of all, there is a definite relationship of this condition to diseases of the liver, particularly to those in which there is liver insufficiency. As might be expected, therefore, the condition develops in old people as well as in younger ones. This association suggests very definitely that changes are of an acquired rather than an hereditary character. Secondly, the condition has been observed to occur after injections of œstrogens (Bean, 1945). The cases concerned have been principally ones of carcinoma of the prostate treated for relief of pain or in order to diminish the rate of growth of the tumour by such injections. Not only have telangiectases appeared after these, but they have disappeared when the injections have been stopped, only to reappear again when they were resumed. This phenomenon can be integrated with the occurrence of telangiectases in liver disease, because it is known that the damaged organ does not adequately carry out the normal liver function of metabolizing œstrogens. It is assumed that, since œstrogens will not be destroyed in the normal manner, therefore there will be a greater amount of them present in the body. It is this accumulation of hormone that produces the same effect as œstrogens given by injection. Thirdly, these observations may be correlated also with the occurrence of telangiectases in pregnancy.

3. It appears, from a few observations, that certain substances such as rutin may have some influence on the course of the condition.

[1] *"Man wird betrogen, man betrügt sich selbst."*—GOETHE, *Sprüche in Prosa*, iii.

Thus the vascularity does not appear to be a fixed one, due to some genetic peculiarity, but rather one associated with clearly defined environmental changes, in this case a chemical one. It should be noted that in this way what is necessarily, in the present state of knowledge, a vague concept is replaced by one which not only is relatively precise but also is capable of direct observation and experimental confirmation.

It is apparent that the general viewpoint is changing. What is stated here is not new, but the older idea is still sufficiently widely held to justify some emphasis of newer ideas. Much of the information has been obtained from biochemists and special investigators, but the easily observable clinical features are such as to give pause to one's carefree acceptance of the current view. This is important also because of its bearing on the nature of conditions discussed subsequently.

Varicose Veins.

We may now turn to a condition observed much more frequently; in fact, it is an observation which may be made daily in an out-patient department in any large hospital. We are inclined, I think, to regard the conditions that we see frequently as being of less interest and perhaps even less importance than the ones that we see rarely. Nevertheless, we should heed the exhortation of Pliny the Elder: "Let no things, because they are common, enjoy the less share of our consideration." (*"Historia Naturalis"*, Book XIX, Section 59.) Indeed, we should remember, with Emerson, that the "invariable mark of wisdom is to see the miraculous in the common". If we should happen to have this "mark of wisdom" we are able to examine these cases very frequently, and, as we shall see, the more carefully we consider the common things, the more we find them to be worthy of our attention.

The general view about varicose veins is, so far as their origin is concerned, that they are due to weakness of the walls (probably hereditary) and that the varicosities arise because of increased venous pressure due to back flow from the proximal veins. This back flow is possible because of loss of competence of the valves of the veins. These opinions are accepted almost universally without any question whatever; but if we examine affected patients carefully we find that there is every reason to suggest that this very superficial, even though common, point of view does not conform with easily made observations.

Most of the varicosities seen—for example, in patients in an out-patient department—are ones that have been in existence for many years; so we are seeing the late stages of the condition. There is no question that the appearances at this stage probably do not have any direct bearing on the early changes, but at the same time this point of view is not generally recognized. Nor is it appreciated that the observations made on the grossly changed structures must be checked carefully against those made at other stages before conclusions are drawn.

When varicosities in young people or, irrespective of age, those occurring at an early stage are investigated, it is found that they occur as little groups of dilated veins which do not necessarily have a direct relationship to the large proximal veins. They occur often as a little bunch of veins—for example, near the knee—and there is a normal vein (normal in calibre and with regard to its valves) between this and the larger vessels.

At this stage it may be noticed that there is a swelling of the veins in the region of the valves. This is said often to be proximal to the valves, on the argument that an important factor in the development of varicosities is back pressure in the main veins. At the same time, if this dilatation is proximal to the valves it means that the valves are competent; and yet an important part of the hypothesis, mentioned above, concerning the development of these varicosities is that the valves are, or become, incompetent. Actually, if the veins are examined carefully it is found that this dilatation is distal to the valves rather than proximal to them.

Pulsation is sometimes to be seen in the veins, and if this is investigated carefully, it will be found that it is

not a pulsation back from the veins, but, as can be shown by pressure on the veins proximal to the varicosities, is due to a centripetally transmitted impulse. Another point is that the blood in the veins can be demonstrated to contain more oxygen than usual. This simple observation may be made during operation; it will be seen that the blood in the veins is bright red in colour rather than the bluish colour that one might expect and indeed often sees in other veins. This can be determined most satisfactorily when an operation is performed under local anæsthesia—that is, when complicating factors due to general over-oxygenation or under-oxygenation are absent.

An important feature is a well-defined histological peculiarity of these veins. In the outer part of the wall and in the tissue immediately peripheral to the veins, there is a large number of capillaries and vessels of capillary and arteriolar size. It should be mentioned here that attention was directed towards this phenomenon as a result of interest in the clinical observations mentioned above. It is quite clear that they suggest that the important factor in the development of varicosities is, at an early stage, the transmission of a larger amount of blood than usual into a segment of the veins from the arterial side rather than from the larger veins. The histological demonstration of the many small vessels seen, resembling those seen in cases of obvious arterio-venous communications and providing as they do a path by which the blood may pass rapidly and easily from the arterial to the venous side, supports this view.

The general proposition of the development of varicose veins as a special type of arterio-venous shunt formation has been put forward in a current paper (King, 1950*b*). The question is raised here and discussed because this development of varicose veins is an important aspect of a widely applicable principle.

It has been shown that the development of varicosities is associated with the presence of an increased amount of hormone of the œstrogen type. Precise information is not yet available; neither is it known which member or members of the œstrogen group may be responsible for the changes nor the way in which the œstrogens may act. Nevertheless, the clinical observations that have been gradually collected and the experimental work that has been done indicate that in the early stages the development of this change in the vessel wall is due to such a chemical stimulus or series of stimuli (which gives rise to the arterio-venous shunt—just as in the telangiectases) rather than to some general mechanical factors.

It should be noted here in passing that in the late stages of the condition, when there is a well-developed deformity of the veins—lengthening, tortuosity and dilatations—the mechanical factors are important; but in the early stages to which we have been referring these play an insignificant role.

Here we have a new and definite orientation of our observations—a segregation of those made at an early stage from those of the later stages—with a corresponding simplification and clarification of our deductions. "Yes, all things without exception, because of symmetry, will appear more beautiful when placed in order." (Xenophon: "Economics", VIII, 19.)

We can see here, therefore, that the general viewpoint regarding the origin of this condition is also gradually changing. This has become apparent by the application and integration of several kinds of observation, but it is clear, in retrospect, that the general direction in which our studies would lead us are indicated by simple clinical observations. Indeed, some of these were made many years ago (Ledderhose, 1906; Hasebrök, 1916) but have been given inadequate attention.

Hydronephrosis and Hydroureter.

Hydronephrosis and hydroureter—dilatation of the ureter and its pelvis—are frequently associated with changes in the lower part of the urinary tract, in which either there is a definite obstruction of the tract or else there is some condition which is very easily interpreted either as being an obstruction or as causing one. Thus we see them frequently in cases of enlargement of the prostate and in some cases of pregnancy. The former will be discussed later in some detail, so we will confine our attention here to the second condition.

It has been stated frequently, and is still stated in some text-books, that this dilatation of the ureter is due to obstruction of the lower part by the enlarging uterus. One thing is clear: there is enlargement of the ureters in some cases of pregnancy, but beyond this there is little definite positive evidence. Indeed, if we consider the cases carefully, we find that often there is a well-developed hydroureter at a stage when the uterus itself could not have caused mechanical pressure.

In this regard the hydroureter is related to those varicosities which develop in early pregnancy. These are usually said to be due to pressure of the enlarging uterus on the veins in the pelvis, but a careful history and an adequate examination show that the dilatation of veins occurs in places where such pressure, even if it did occur, is not likely to have been effective or to have produced the particular changes observed. This distribution, combined with their formation at a stage when the uterus is still small, makes the mechanical idea untenable as a complete explanation.

This idea of the preeminence of the hormonal factor, like others that have been mentioned, is not new. Thirty years ago it was suggested by the urologist Kidd (1920) that the dilated ureters of pregnancy were due to the action of some chemical substance in the blood and not to mechanical obstruction. This notion, however, does not seem to have received any significant amount of attention, and judging by the literature has been considered by only a few investigators.

The study of this aspect of the problem has been left largely to the experimenters; thus we see that the injection of œstrogens is followed by dilatation of the ureter (Hundley *et alii*, 1942), and it was shown to occur with hydronephrosis, together with distension of the urinary bladder. Hydronephrosis was observed following the injection of œstrone in mice (Burrows and Kennaway, 1934). Observations on bladder dilatation in mice after the injection of œstrin have been recorded also by Weller *et alii* (1936). They showed that there are important differences in the effects of one substance on different genera. The importance of the chemical factor in the pyelitis of pregnancy has been emphasized by Burrows (1936).

This distension of parts of the urinary tract in human beings may be correlated not only with the results of experimental observations but also with the development of varicose veins (either naturally occurring or as influenced by hormone injection). It is not proposed to discuss this here in detail, but merely to indicate that the distension of muscular tubes, irrespective of their contents, should be regarded as a general proposition.

Enlargement of the Prostate.

Enlargement of the prostate, like varicose veins, is to be found very frequently, and consequently its general features are well known. We shall briefly consider these first. It should be noted that, as with varicose veins, it is the well-developed stage of the disease, the stage at which signs and symptoms, some of which are due to complications, are clearly defined, that is given prominence.

There is usually an easily demonstrable enlargement of the prostate itself. Even if this is not clearly apparent clinically, it is shown during treatment—for example, at operation. Associated with this there is distension of the bladder, and before very long there are changes in the bladder wall consisting of trabeculation and thickening of the wall. It is to be noticed, of course, that the thickening may not be apparent when the bladder is distended. Associated with the distension are hydroureter and hydronephrosis. For the moment I do not propose to consider complications such as the development of infection (important though this may be clinically) or the formation of calculus.

This so-well-known condition, affecting as it does some of the most influential members of the community, has attracted very great attention (doubtless partly because of the individuals affected), and naturally many attempts

have been made to explain its development. At the beginning of this century there were no fewer than fourteen well-known hypotheses as to its nature. These ranged from the idea that it was a tumour (for what such an idea was worth at a time when the nature of neoplasms was still uncertain) to the notion that it was an attempt on the part of Nature to provide a stimulus to weakening muscular structures. So far as the second is concerned we have now grown out of, or are growing out of, such futile teleological conceptions, and these are being replaced by much more objective hypotheses.

It can now be accepted that the proliferation of prostatic tissue which constitutes the enlargement of the gland is due to chemical stimulation, the substances responsible being of the œstrogen group. The evidence for this is partly clinical (that enlargement of the organ is found in newborn babes, and that enlargement occurs when secretion of testosterone is diminishing and that of the œstrogens is increasing) and partly experimental (that enlargement of the organ can be shown to follow regularly the injection of œstrogens into animals, including man).

The general relation of enlargement of the prostate to the other phenomena we have mentioned, distension of the bladder as well as hydronephrosis, is almost universally regarded as one of cause and effect. The general view is that the enlargement causes obstruction to the urethra, either in the prostatic portion or at the internal meatus (by a middle lobe), and that the distension of the bladder, the trabeculation, the formation of diverticula and the ureteric changes are the mechanical results of this obstruction. This is the point to which we will now give attention.

When early cases of prostatic enlargement are considered carefully several features are demonstrable.

1. Difficulty of micturition is noted at an early stage of the development of the disease and often before the actual prostatic enlargement is demonstrable by any ordinary means. This may be so for a considerable time, even several years.

2. The difficulty of micturition may be associated with even quite small prostates. We are not considering for the moment cases of fibrous prostate, cases of obstruction of the bladder neck said to be due to an Albarran bar or the pin-hole internal meatus.

3. Frequency and precipitancy of micturition are not easily explicable as a direct result of urethral obstruction, particularly at an early stage.

4. When retention of urine occurs it is usually found that the passage of a simple rubber catheter is all that is necessary to relieve the "obstruction".

5. When a catheter has been passed in these cases it is found that the urine passes out very slowly. It seems quite clear that the contractility of the bladder wall is grossly altered. It should be noted that this occurs in some of the early cases—an important feature, because it is usually said that this phenomenon is due to over-distension of the bladder and over-stretching of the muscle.

One point that never receives adequate attention is that much of the argument about the distended bladder and residual urine is based on the completely misconceived notion that the laws relating to the stretching and fatigue of striated muscle can be applied directly and without modification to smooth muscle. If we pause to consider that striated muscle fibres are attached at their extremities to other structures, whereas smooth muscle fibres have not such an attachment and slide over each other, it becomes apparent that some of the simple "explanations", derived by analogy with skeletal muscle, are inadequate.

When we examine subjects of prostatic enlargement *post mortem* we find that there are features which do not conform easily with the usual hypothesis.

1. The lack of correlation between the size of the prostate and the symptoms described in the histories is even more apparent than it was clinically.

2. The size of the urethra is quite striking; it is often voluminous. There may be projections of a lobule or lobules into the urethra, but usually these are not sufficiently gross to cause actual obstruction. There may be a well-defined middle lobe, but this, more often than not, clearly is incapable of causing any obstruction. The lobe on the narrow pedicle which can act as a "ball valve" is uncommon. It must be recognized that obstruction is demonstrably present in some cases, but even at the late stages, as seen at post-mortem examination, this does not apply to the majority.

3. There is lack of correlation between the size of the prostate and the degree of change in the bladder wall.

4. There is a complete lack of correlation between the prostatic size on the one hand and either any demonstrable interference with the urethra or the degree of hydroureter on the other.

In view of these features it is difficult to accept any simple mechanical relationship between the prostatic enlargement and the bladder and ureteric changes. It should be emphasized that it is intended to suggest not that mechanical factors play no part here, but that they do so at a late stage. For an explanation of the early stages we must look elsewhere.

Here the experimental work mentioned earlier is important. Bladder dilatation and hydroureter as the result of injection of œstrones in animals and hydroureter in pregnancy are important. These, combined with the evidence that enlargement of the prostate is the result of œstrogen activity, reorientate the two conditions to each other. As a colleague of mine suggests, they become cousins instead of being father and son.

Here again we have the change in viewpoint—from the simple mechanical idea to that involving chemical agents. The demonstration of these is a matter for the skilled biochemist, and he is still investigating them; but as was noted with other conditions, there are sufficient easily demonstrable clinical observations to indicate that mechanical factors do not account for many features of the condition and to throw doubt on the commonly accepted view of their place in the natural history of the disease.

Intestinal Dilatations.

The group of intestinal dilatations comprises several conditions, some of which are well known, others of which are not so well appreciated. In the first class come Hirschsprung's disease, megaduodenum and achalasia of the cardia of the stomach. The second class comprehends a miscellaneous collection, such as localized dilatations of parts of the colon (as are sometimes encountered by surgeons when an organic stricture is expected) and localized dilatations of varying extent occurring in parts of the small gut. These last range from areas of dilatation of about three or four inches in length up to those which involve several loops of intestine.

These have all been the subjects of continuous polemics, not yet resolved, over the last three-quarters of a century, on whether they are due to some organic obstruction or whether it is a matter of disturbance of the nerve supply to the gut—a neuro-muscular incoordination.

Despite recent statements supporting the mechanical notion, it can be said that the consensus of evidence is in favour of the view that these are due to some neuro-muscular disturbance rather than to a distinct mechanical stricture. Of course, mechanical factors may be present in the late stages, as they are with other conditions, but these should not be confused with the essential or initiating lesions.

It may be noted here that these conditions may be associated with disturbances of the urinary tract, such as hydroureter and hydronephrosis. This association is not common, but occurs sufficiently frequently for us to suggest that they may be related in their cause. This would suggest, then, that the exciting factor in this dilatation of the bowel may be a chemical stimulus, just as it seems to be in at least some of the cases of dilatation of the ureter. This does not necessarily cut across or contradict the idea of a disturbance of the neuro-muscular mechanism. Instances of chemical action on muscle by way of the nerves or nerve endings are well known. However, in

this instance the hypothesis waits on more detailed information.

The important thing here is that we have a condition which was, not so very long ago—and still is, according to some recent writers—considered to be due to some definite mechanical cause. I do not propose to go into details of available information indicating that a mechanical factor is an inadequate explanation. Here again simple direct observation, such as may be made at operation, shows that there is a distinct functional alteration in the bowel, but without any indication of a constant morphological change such as a fibrous stricture.

Another group of conditions related to these is that of the diverticula of the small intestine. One of the characteristics of these, at an advanced stage, is the occurrence of attacks of pain and constipation. These are frequently associated with dilatations of the bowel. It is usually assumed that these dilatations, which are topographically related to the diverticula, are secondary to (that is, complications of) these structures. However, even if the two do not occur simultaneously, they are closely related and due to a common factor. This question has been discussed in a recent paper (King, 1950*a*).

It is not possible to deal with this subject adequately here, but it is of special interest because some writers have suggested that these conditions are related to weaknesses of the abdominal wall (Beer) and form a connecting link between the bowel dilatations and some herniæ of the abdominal wall.

Hernia.

The last subject which we will discuss is that of hernia, of which probably the best example, because it is the most common, is the inguinal type.

Practically all attention has been focused on the mechanical side of the development of inguinal hernia. This is not only because we seem always to be attracted first by mechanical explanations, but also because of the surgeons' interest in it, and incidentally since so many herniæ (post-operative) are due to mechanical interference; and in recent years attention has been directed increasingly to this condition as a medico-legal problem in workers' compensation cases.

Nevertheless, in comparative anatomy, physiology and pathology we have considerable evidence which should give us pause, when we consider that all herniæ, particularly those which develop spontaneously in early life or in people with good muscular abdominal walls, are due to simple mechanical pressures. I refer to those animals in which it is known that the testes descend into the scrotum at certain times of the year and that a pouch of peritoneum descends with them.

The unsatisfactory character of raised intraabdominal tension as an explanation of the development of a hernia is reflected in the numerous (sometimes heated) discussions that have occurred round this point. It is necessary to say here only that the problem of hernia—that is, of a group of spontaneously developing herniæ in young people (because it is known that some herniæ are definitely traumatic or mechanical in origin)—is now being considered from the point of view of the possibility that this change is due to a chemical stimulus[1] rather than to a simple *vis a tergo* from the abdominal cavity.

I know that it will be some time before the problem is clarified. This will necessarily be so because there is still much confusion between the spontaneously occurring herniæ (especially the one that is called congenital) and that which is definitely due to or is precipitated by mechanical stresses. Nevertheless, it is one which must receive its due share of attention in view of the changing point of view.

Conclusion.

From consideration of the somewhat heterogeneous group of conditions which we have discussed this evening, we may derive some general ideas. The current hypotheses as to their nature are quite inadequate and in many ways do not deal with them realistically, either clinically or pathologically. They deal with late results and not with causes, and therefore cannot be of any real value in treatment; indeed, treatment based on them can be of only temporary value, and this is shown by the poor results so frequently achieved in the treatment of conditions such as varicose veins and hernia. They depend on insufficient observation. They demand that easily demonstrable phenomena be ignored. They ignore all the recent special chemical work and the implications of this. They ignore the general trends in modern attacks on pathological problems. They belong to a rigid morphological, indeed "dead" era; to the time when, with some justification, pathology was regarded as being the study merely of dead tissues. This was an important, in fact an essential, phase in our development, but necessarily an evanescent one.

That pathology is merely a study of morphology has ceased to be true. Pathology is the study of disease irrespective of method, and furthermore many methods such as those of histochemistry, submicroscopic physics and the like are being increasingly used; but in addition the clinician can be a pathologist as well as the morbid anatomist or the physiologist. One point that I have wished to make this evening has been that clinical observation—the observation of the living organism—is most important in elucidating pathological problems, and of course here the clinician is the pathologist—the student of the abnormal. Statements of this kind have been made often, but since they are usually not adequately appreciated, repetition is necessary.

If we are to keep pace with our contemporaries in other fields, and indeed ourselves remain mentally alert, then we must always be prepared for changes. When we replace a mechanical notion of causation with a chemical one, one problem is only being replaced by another; but, as Sir Harry Allen used to say, "what we can hope for is merely to be able to push back a little further the curtain that hides the unknown". If we can add our own small share, then we can take our place amongst those investigators who are really alive; and the clinician can add his quota just as surely as the individual who is working in a laboratory.

The study of the particular problems that we have discussed this evening emphasizes that often unobtrusive but general truth that it is not possible to stand still. If we are not to retrogress and atrophy we must advance. We know, with Robert Browning (*Paracelsus*, Part V), that "progress is the law of life".

[1] This is easily demonstrated in mice, but has not yet been proved for other animals (Burrows, H., 1945, "Biological Actions of Sex Hormones", Cambridge).

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HYPOKALÆMIA COMPLICATING SODIUM PARA-AMINO-SALICYLATE THERAPY FOR PULMONARY TUBERCULOSIS.

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EXCEPT for a recent report of three cases (Cayley, 1950), no published information concerning the development of hypokalæmia during para-amino-salicylic acid therapy has appeared. We have found it a frequent complication when the sodium salt has been given, and although the manner of development of this electrolyte deficiency has not been elucidated, this preliminary report is made because of the serious nature of this complication, and the fact that the outcome may be fatal.

States of hypokalæmia have been observed in many unrelated diseases, notably familial periodic paralysis, diabetic coma, chronic nephritis, biliary and intestinal fistulæ and Cushing's syndrome, and in cases of Addison's disease treated with large doses of desoxycorticosterone (Danowski, 1949).

In such states of potassium deficiency muscular paralysis may supervene in the form of flaccid paresis of the trunk and extremities of a variable extent and degree, and in the more severe cases it may involve the diaphragm and intercostal muscles with ensuing death from respiratory failure.

In conjunction with this muscular insufficiency, or indeed in its absence, the cardio-vascular system is frequently involved. Characteristic circulatory phenomena include (i) cardiac irregularity due to multiple premature systoles, (ii) cardiac dilatation with high venous and pulse pressure, and (iii) sudden death which, in the absence of evidence of muscle paralysis, may be assumed to be due to ventricular fibrillation or arrest. With a fall in the serum potassium level characteristic changes appear in the electrocardiogram. The *S-T* segment becomes depressed and the *T* wave flattened and broadened (Frenkel *et alii*, 1947).

All the evidence available at present suggests that the muscular and cardio-vascular systems bear the brunt of those disturbances of electrolyte balance characterized predominantly, though not necessarily exclusively, by a lowering of the serum potassium level. In the course of this study, we have employed the colorimetric method for the estimation of potassium, using the Folin-Ciocalteu phenol reagent (Abul-Fadl, 1949), and we have regarded 16 milligrammes per 100 millilitres as the lower level of normal.

Table I presents the salient features of our cases of hypokalæmia. The cases are grouped according to the following plan: (i) six proved cases, in which biochemical and electrocardiographic abnormalities and/or signs and symptoms were present; (ii) two cases in which there was clinical evidence only; (iii) two cases in which biochemical changes were present; in one no electrocardiogram was taken; in the other the record was abnormal at a time when the serum potassium content was within normal limits; (iv) two cases of sudden death; in one the electrocardiographic findings were suggestive of hypokalæmia.

REPORTS OF CASES.

The patients in this series were suffering from active extensive pulmonary tuberculosis and were febrile, and their sputum contained tubercle bacilli.

CASE I.—A male patient, aged fifty-seven years, was admitted to hospital on October 21, 1949. Prior to the commencement of treatment with sodium para-amino-salicylate on February 11, 1950, his pulse was irregular owing to the presence of auricular premature beats. The electrocardiogram was normal and the serum potassium content was 21·0 milligrammes per 100 millilitres. In the first two weeks of treatment abdominal discomfort was experienced. During the third week he had pains in the shoulders, elbows and knees and a rise in temperature. These pains had almost subsided by the twenty-first day of treatment (March 3), when it was found that his serum

TABLE I.

Case Number.	Date of Commencement of Treatment.	Dosage of Sodium Para-amino-salicylate.	Days of Treatment Prior to Onset of Hypokalæmia.	Symptoms and Signs.	Electrocardiographic Changes.	Serum Potassium Content. (Milligrammes per 100 Mils.)	Time Taken for Recovery.	Result.	Post-Mortem Findings.
I	11.2.1950	12 grammes per day 6 days per week.	21	Generalized joint pains, pulse irregularity.	Present.	10	5 days.	Satisfactory.	
II	8.2.1950	12 grammes per day 6 days per week.	52	Muscular weakness, *pulsus bigeminus*.	Present.	12	5 days.	Satisfactory.	
III	2.1.1950	12 grammes per day 6 days per week.	60	Muscular weakness.	Present.	10·3	14 days.	Satisfactory.	
IV	4.3.1950	12 grammes per days 6 days per week.	22	Drowsiness, multiple extrasystoles.	Present.	12	—	Death.	Pulmonary tuberculosis; no other significant findings.
V	23.3.1950	12 grammes per day 6 days per week.	13	Drowsiness.	Present.	6	3 days.	Satisfactory.	
VI	13.2.1950	12 grammes per day 6 days per week.	48	Muscular weakness.	Present.	15·3	2 days.	Satisfactory.	
VII	29.10.1948	15 grammes per day.	29	Muscular weakness, incontinence of urine.	—	—	—	Death.	Pulmonary tuberculosis; toxic changes in liver and kidneys.
VIII	14.5.1949	15 grammes per day.	51	Muscular weakness, flaccid paralysis.	—	—	14 days.	Satisfactory.	
IX	21.9.1949	15 grammes per day.	29	Toxic jaundice, erythematous rash.	No electrocardiogram taken.	13·3	—	Satisfactory.	
X	17.8.1949	15 grammes per day.	54	Nil.	Present.	14·0	—	Satisfactory.	
XI	3.5.1949	15 grammes per day.	44	Coupled beats.	Present.	—	—	Death.	Pulmonary tuberculosis with extension to the bowel; myocardial infarct.
XII	13.12.1948	15 grammes per day.	27	Nil.	—	—	—	Death.	Extensive pulmonary tuberculosis.

potassium level had fallen to 11·6 milligrammes per 100 millilitres. His pulse was more irregular than previously, but he showed no muscular weakness. His mouth was rather dry and his sputum was sticky and hard to raise. In retrospect he noticed some mental dulness. Sodium para-amino-salicylate therapy was continued, and the serum potassium level continued to fall, being 10·0 milligrammes per 100 millilitres on March 6 and 8·3 milligrammes on March 9. An electrocardiogram taken on March 9 showed gross arrhythmia due to frequent premature systoles and *ST-T* segment changes consistent with the presence of potassium deficiency (Figure IV). Without suspension of the sodium para-amino-salicylate therapy, potassium chloride was administered orally for two days. The serum potassium levels were 11·2 milligrammes per 100 millilitres on March 10 and 7·9 milligrammes on March 11. The dose of potassium chloride was increased, 56 grammes being given during the next three days. The serum potassium level was 11·5 milligrammes per 100 millilitres on March 12, 15·4 milligrammes on March 13 and 20·5 milligrammes on March 14. Another 42 grammes of potassium chloride were given during the next two days, and then potassium chloride and sodium para-amino-salicylate therapy was suspended and potassium para-amino-salicylate therapy commenced.

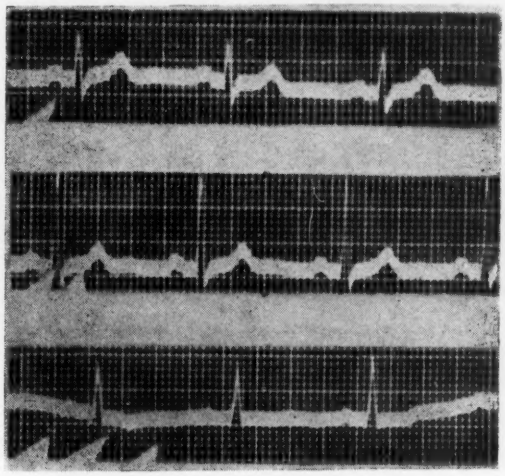

FIGURE Ia.

Case II. Before treatment. Electrocardiogram within normal limits.

The serum potassium level has remained above 20 milligrammes per 100 millilitres during the last month of this treatment. Serial electrocardiograms reflected closely the changes in the serum potassium level, and when this returned to normal the arrhythmia and the characteristic *ST-T* segment changes disappeared.

CASE II.—A male patient, aged thirty-eight years, was admitted to hospital in January, 1950. In spite of bed rest at first, and later streptomycin therapy, the disease continued to spread. Sodium para-amino-salicylate was accordingly prescribed in addition, and its administration was commenced on February 8, when the electrocardiogram was within normal limits and the serum potassium content was 22·8 milligrammes per 100 millilitres. During the following fortnight the patient complained of some anorexia and nausea and on March 21 of mild pain in the left arm and right elbow. On the evening of April 4 he noticed transient weakness of the left arm. He was examined shortly afterwards, but power had then returned and the reflexes were present. He had a *pulsus bigeminus*. His serum potassium content was 12 milligrammes per 100 millilitres. An electrocardiogram taken the following morning showed changes consistent with hypokalæmia, but the cardiac rhythm had returned to normal (Figure I). Sodium para-amino-salicylate therapy was suspended, and large doses of potassium chloride were administered, 24 grammes being given on April 5 and 48 grammes on April 6. The serum potassium content was 15 milligrammes per 100 millilitres on April 6, but had fallen to 9·3 milligrammes per 100 millilitres on April 7. By April 11 it had risen to 26 milligrammes per 100 millilitres after a further 36 grammes of potassium chloride had been given. The electrocardiographic changes returned to normal and the patient felt better and more alert.

CASE III.—A male patient, aged twenty-eight years, was admitted to hospital on November 30, 1945. In addition to extensive bilateral tuberculous disease he had mild hypochromic anæmia which failed to respond to treatment, and recurrent dyspepsia for which no cause was found.

Sodium para-amino-salicylate therapy was commenced on January 2, 1950, when his serum potassium content was 21·3 milligrammes per 100 millilitres. An electrocardiogram was within normal limits on January 17, his serum potassium content on that day being 17 milligrammes per 100 millilitres. During the first month he experienced mild abdominal discomfort. On January 31 his serum potassium content was 19·3 milligrammes per 100 millilitres. After this date he complained of increasing anorexia and nausea with occasional vomiting. Abdominal discomfort was not relieved by food or alkalis and was worse after fatty foods. The liver edge was palpable, and he was regarded as suffering from mild hepatitis. His temperature rose to 100° F., and he complained of headache on waking in the mornings, was restless, with aching pains in the legs and shoulders, and

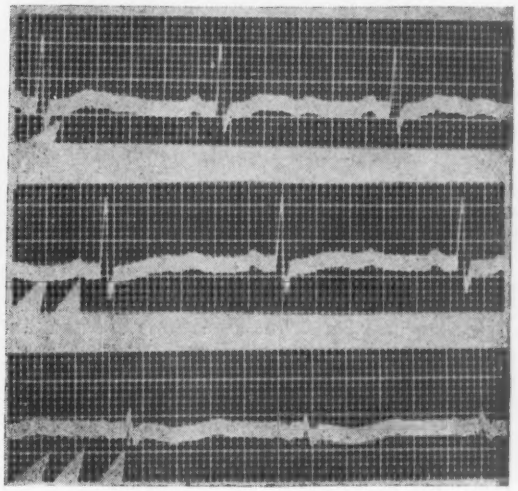

FIGURE Ib.

Case II. Serum potassium level 12 milligrammes *per centum* (April 4, 1950). Slight *S-T* depression, Lead II. *T* wave in Leads I and II broad, notched and flat. *U* wave present. *T* wave in Lead III inverted—broad, smooth and shallow. Compare with *T* wave in Lead III in Figure Ic.

found it difficult to sleep. On February 20 his mouth was dry and a small ulcer developed on the lower lip. On February 22 he noticed slight weakness of the limbs. Oral sodium para-amino-salicylate therapy was suspended on February 24, being replaced by aerosol administration which provided one gramme of sodium para-amino-salicylate daily and which was continued until March 4. Whilst he was still receiving the drug by aerosol the weakness of the limbs increased, particularly that of the legs, and on February 25 he experienced difficulty in rolling over in bed. Power in all limbs was grossly diminished, especially in the quadriceps muscle. On February 27 the serum potassium content was 10·3 milligrammes per 100 millilitres, and the electrocardiogram showed changes consistent with potassium deficiency (Figure IIb). The weakness of the limbs fluctuated, but decreased gradually, and full power returned in fourteen days. During this time the serum potassium estimations gave the following results: March 1, 12·8 milligrammes per 100 millilitres; March 2, 16·8 milligrammes per 100 millilitres; March 3, 14·0 milligrammes per 100 millilitres; March 8, 15·6 grammes per 100 millilitres; March 10, 16·0 milligrammes per 100 millilitres. On March 10, as the serum potassium level was at the lower limit of normal, 12 grammes of potassium chloride were given daily for two days. After the first day the serum potassium level rose to 25·8 milligrammes per 100 millilitres. The electrocardiographic changes reflected the serum potassium levels and

returned to normal with the serum potassium content (Figures IIA, IIB, IIC and IID). On March 20 para-amino-salicylate therapy was recommenced with the potassium salt. The patient has since remained well.

Case IV.—A male patient, aged seventy-two years, was admitted to hospital on November 14, 1949, and the administration of sodium para-amino-salicylate was commenced on March 4, 1950, when his serum potassium content was 12·5 milligrammes per 100 millilitres and his electrocardiogram was within normal limits, although some premature systoles were present. Because of vomiting during the first few days of treatment, sodium para-amino-salicylate was suspended for ten days, and was recommenced on March 16. Apart from abdominal discomfort he tolerated the drug well. On April 4 he became drowsy, and the arrhythmia was more pronounced. An electrocardiogram at this date showed an increase in the number of premature systoles and the characteristic *ST-T* segment changes (Figure IIIB), and his serum potassium content was 12 milligrammes per 100 millilitres. There was no muscular weakness, and examination of his nervous system revealed no abnormality. His

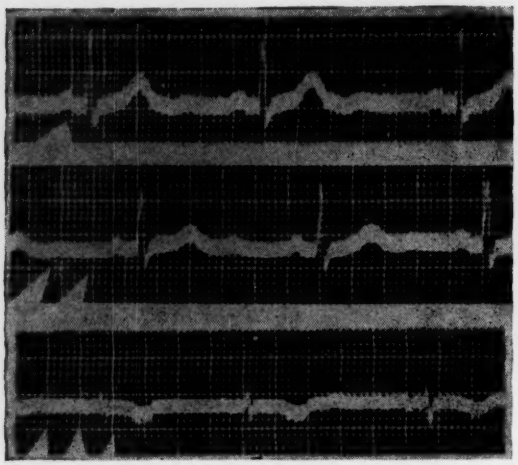

Figure Ic.

Case II. Electrocardiogram within normal limits. Serum potassium level normal.

blood pressure was 140 millimetres of mercury (systolic) and 50 millimetres (diastolic), his hands were warm, and there was no evidence of congestive failure. His sputum was sticky and difficult to raise. Sodium para-amino-salicylate therapy was suspended and potassium chloride was given in a dose of six grammes every four hours. On being awakened the next morning for the fourth dose of potassium chloride, he sat up to take the mixture, collapsed and died suddenly.

This patient's serum potassium level was low, he had gross arrhythmia, and his electrocardiogram showed the characteristic changes associated with a low serum potassium level (Figure III). An autopsy failed to reveal adequate cause for death, and it is concluded that he died as the result of hypokalæmia.

Case V.—A male patient, aged fifty-four years, was admitted to hospital in January, 1950, and the administration of sodium para-amino-salicylate was commenced on March 23. The serum potassium level was not estimated and no electrocardiogram was taken prior to treatment, during which he experienced anorexia, nausea and abdominal pain. On April 5, a fortnight after the commencement of treatment, the serum potassium content was 6·0 milligrammes per 100 millilitres, and the electrocardiogram showed changes consistent with hypokalæmia. He was given 26 grammes of potassium citrate on April 5, 24 grammes of potassium chloride on April 6 and 12 grammes of potassium chloride on April 7. On April 6 the serum potassium content was 15 milligrammes per 100 millilitres, and on April 7 it was 20 milligrammes and the electrocardiogram was normal. He felt better and became more alert.

Case VI.—A female patient, aged twenty-eight years, was admitted to hospital on January 9, 1950. During the first month she remained febrile and the disease extended. Sodium para-amino-salicylate therapy was commenced on February 13, when the *T* waves in the electrocardiogram were of low voltage, but the tracings were otherwise within normal limits. The serum potassium content on March 15 was 21·3 milligrammes per 100 millilitres. The patient tolerated the drug fairly well, apart from some looseness of the bowels, but on April 2 noticed slight weakness in the legs and arms. This weakness became more pronounced during the subsequent few days, and her muscles ached. The serum potassium content on April 6 was 16 milligrammes per 100 millilitres. By April 11 power in all limbs was much diminished, especially in both arms and the left leg, the muscles ached and the forearm muscles felt firm and doughy. The biceps and triceps reflexes were difficult to elicit, particularly in the left arm, but the knee and ankle reflexes were present. The serum potassium content on April 11 was 15·3 milligrammes per 100 millilitres, and the electrocardiogram showed the typical changes in the *ST-T* segment associated with hypokalæmia. Sodium para-amino-salicylate therapy was suspended on April 11 and she was given potassium chloride, six grammes every three hours. On

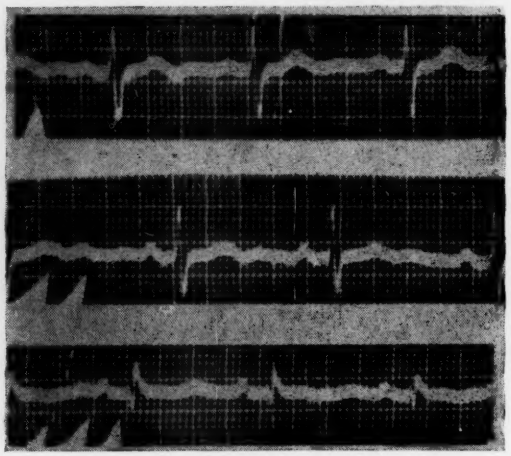

Figure IIa.

Case III. Before treatment. Electrocardiogram within normal limits.

the following day the serum potassium content was 19·5 milligrammes per 100 millilitres and strength had returned to her limbs, although aching pains in the muscles persisted for a further few days and then disappeared. The electrocardiographic changes returned to normal. This patient has maintained her improvement.

Case VII.—A male patient, aged forty-two years, was admitted to hospital on May 29, 1947. Sodium para-amino-salicylate therapy was commenced on October 29, 1948. During administration of the drug his red cell count steadily fell from 3,250,000 to 2,300,000 per cubic millimetre, and on the twenty-ninth day he complained of increasing weakness in his legs. Examination confirmed this weakness; the deep reflexes were present but weak. The following day he complained of sudden loss of power in both arms, and was unable to lift them or to hold them against gravity, although he could perform finger movements if his wrists were supported. All deep reflexes were present, but were very weak. During the next forty-eight hours the limb reflexes were lost, the plantar response remaining flexor in type, and although he was not dyspnœic, he had repeated episodes of hyperpnœa. On the thirty-fourth day there was almost complete paralysis of the trunk and limb muscles, but he could use the muscles of the hands and feet if the limbs were supported. His mental condition was clear and he showed no true ataxia. No sensory loss could be discovered, and there was no abnormality of the cranial nerves, the tendon reflexes were present in the arms, but absent in the legs, and the plantar response was flexor in type. He was incontinent of fæces and urine. During the course of a clinical examination he replied to a question intelligently, but collapsed and died suddenly.

The serum potassium level was not estimated and no electrocardiogram was taken in this case. At autopsy, extensive tuberculous disease was present in both lungs, and toxic changes were present in the liver and kidney. No explanation of his sudden death was discovered in the cardio-vascular or central nervous system.

CASE VIII.—A male patient, aged twenty-three years, was admitted to hospital in February, 1949. He was seriously ill, with extensive tuberculous disease involving the right lung. Sodium para-amino-salicylate therapy was commenced on May 17, 1949. On the fifty-first day of treatment he complained of weakness in his limbs and of cramps in both arms and the right leg; he could not sit up unaided, nor could he maintain a sitting posture. He was unable to feed himself or hold anything in his hands. The tendon reflexes were weak in the legs and absent in the arms; the plantar response was flexor in type. No impairment of sensation or of position sense was discovered. He was weak, pale and listless, and vomited every dose of sodium para-amino-salicylate, which was therefore suspended. The blood calcium level and the urinary secretion of creatinine were normal. After three days, during which there was little change in his paresis, he began to improve, and after eight days he could sit up unaided. Within a fortnight full muscular power had returned. The serum potassium level was not estimated, nor was an electrocardiogram taken. However, the clinical history closely resembles that of proved cases of hypokalæmia.

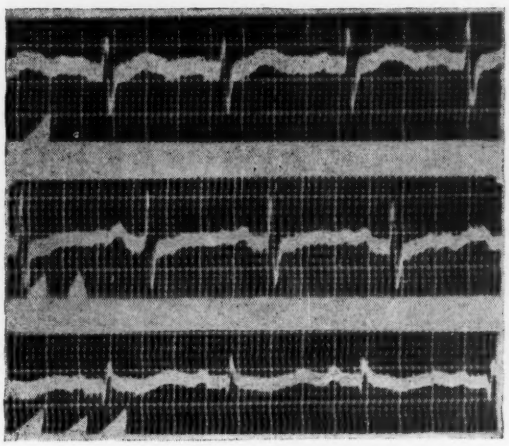

FIGURE IIB.

Case III. Serum potassium level was 10·3 milligrammes *per centum* on February 27, 1950. Lead II characteristic. *S-T* segment depressed, and *T* wave flat, broad and poorly defined. *T* wave in Lead III similar to *T* wave in Lead III in Figure IB—inverted wave is broad, smooth and shallow.

CASE IX.—A male patient, aged fifty-one years, was admitted to hospital in July, 1948. He had previously been given a course of 30 grammes of streptomycin, but the pulmonary disease was progressing. The serum potassium content at the commencement of sodium para-amino-salicylate therapy on December 23, 1948, was 24·1 milligrammes per 100 millilitres. On the twenty-seventh day of treatment his temperature rose, and it continued to rise during the next two days, when his sputum became blood-stained. On the evening of the twenty-ninth day his temperature reached 100·2° F. and an erythematous rash appeared over most of his body. Medication was suspended and he was apyrexial on the thirtieth day, when his serum potassium content was 13·3 milligrammes per 100 millilitres. His temperature rose on three successive days to reach 103·2° F. on the thirty-third day, when he developed liver tenderness and became slightly jaundiced (Van den Bergh test result, four units). Study of his liver function tests suggested toxic hepatitis. Recovery occurred spontaneously.

CASE X.—A male patient, aged thirty-five years, was admitted to hospital in April, 1948. In spite of bed rest his disease was progressing. Sodium para-amino-salicylate therapy was commenced on August 16, 1949, when his serum potassium content was 22·7 milligrammes per 100 millilitres. During the first week of medication he experienced gastro-intestinal discomfort and his temperature rose, and on September 2 his electrocardiogram showed changes suggestive of hypokalæmia, although his serum potassium content was within normal limits—18·2 milligrammes per 100 millilitres. Therapy was suspended. It was recommenced on September 15. On September 26 his serum potassium content was 21·7 milligrammes per 100 millilitres, but at the end of his course on October 20 it had fallen to 14 milligrammes.

This is a case of developing hypokalæmia in which electrocardiographic abnormalities were found incidentally while the serum potassium level remained within normal limits.

CASE XI.—A male patient, aged forty-nine years, was admitted to hospital in June, 1948. He had at times complained of precordial pain, and during an episode of such pain an electrocardiogram was taken, which was within normal limits. Sodium para-amino-salicylate therapy was commenced on May 3, 1949. His general condition improved, but on the thirty-ninth day he complained of diarrhœa and of pain at the lower end of the sternum. Physical examination revealed no cardio-vascular abnormality until the forty-fourth day, when investigation of his pulse revealed coupled beats, and a further electrocardiogram was taken. That night he was found dead in the bathroom. The *pulsus bigeminus* was due to premature ventricular systoles, and the electrocardiogram was more suggestive of potassium deficiency than of myocardial infarction. At autopsy, a fresh septal infarct of small area was found.

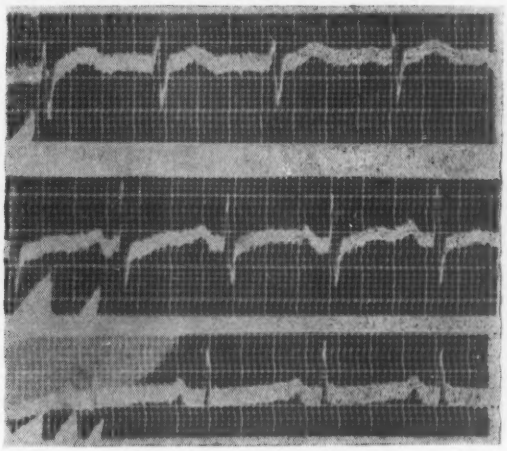

FIGURE IIC.

Case III. Serum potassium content 14 milligrammes *per centum*. Characteristic *ST-T* segment change in Lead II.

The evidence that hypokalæmia was the cause of this man's death is inconclusive and rests solely on the electrocardiographic changes.

CASE XII.—A male patient, aged twenty-six years, was admitted to hospital on February 2, 1948. He had extensive tuberculous disease of the lungs which was not controlled by a left artificial pneumothorax. Sodium para-amino-salicylate therapy was commenced on December 13. He showed no evidence of intolerance to the drug, but it did not influence the course of his disease, and on the twenty-seventh day of the course he was found dead in bed.

Nothing is known of this patient's serum potassium levels, and no electrocardiogram was taken. Autopsy revealed no obvious cause for his sudden death, and the pathologist stated that there was evidence of toxic myocarditis. Therefore hypokalæmia cannot be given as the cause of his death; but it occurred in a manner similar to that in Case IV in which hypokalæmia was demonstrated.

Discussion.

This series of 12 cases occurred in a total of sixty patients suffering from pulmonary tuberculosis who were treated with sodium para-amino-salicylate. Analysis of the figures show that there were six cases of hypokalæmia, in all of which electrocardiographic changes were present, and there was clinical evidence of hypokalæmia in five of these.

Two additional patients developed sufficiently characteristic paresis for the diagnosis to be made clinically. In two other patients an abnormally low serum potassium level developed, although one remained free of symptoms and the second showed evidence of mild hepatitis.

In these ten cases two patients died, one with established hypokalæmia, the second with generalized muscular paralysis strongly suggesting the occurrence of this deficiency. The remaining two cases, although doubtful, are included in the series, because in them the manner of death was in conformity with that which occurs as the result of hypokalæmia. One of these two patients presented characteristic electrocardiographic findings, but at the post-mortem examination a septal infarct was found. The second patient (Case XII) also died without warning, and the autopsy revealed extensive pulmonary tuberculosis, but no adequate cause for sudden death.

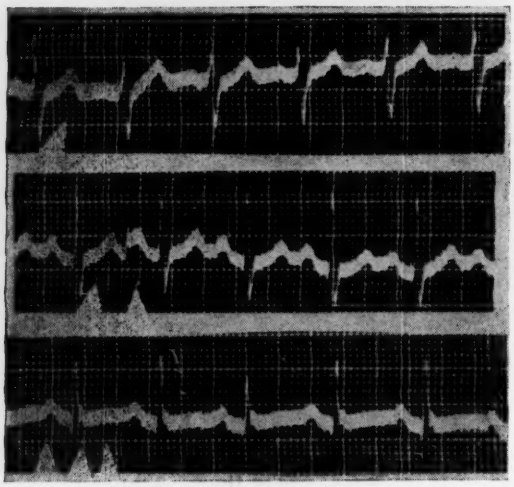

FIGURE IID.

Case III. Serum potassium content 25 milligrammes *per centum*. Electrocardiogram within normal limits.

These observations are consistent with many reports in the literature of sudden death in conditions known to be associated with hypokalæmia.

Analysis of Symptoms.

In five cases there was muscular weakness which varied in degree and distribution. Muscle pain was present and usually persisted for a day or two after power had returned.

In two cases in which the paresis was profound, loss of deep reflexes occurred, whilst in the remainder the reflexes were preserved. In one of these the muscles were firm and doughy.

No definite serum potassium threshold was observed for the appearance of paresis, and the serum potassium level was found to be low in several cases in which paresis did not appear. Several patients were rather drowsy and mentally dull, but this was not pronounced and was noticed by the patients only in retrospect. It is possible that other symptoms, such as gastro-intestinal upset and evidence of liver damage, were due to direct toxic effects of the drug and were unrelated to the hypokalæmia.

Heart and Electrocardiographic Changes.

Electrocardiographic studies in divers cases of hypokalæmia have been described by various authors. The abnormalities noted consist of depression of the *S-T* segment, low voltage of the *T* waves, increase in the *Q-T* interval and the frequent occurrence of *U* waves, together with associated arrhythmias and auriculo-ventricular block. It is our opinion that the most characteristic changes occur in the *ST-T* segment which shows a highly individual configuration in states of gross deficiency.

The *S-T* segment is depressed. In some cases the identity of the *T* wave is preserved (Figure III). It is flat, often notched and always distinctly broadened. In other cases it is only ambiguously defined, rising out of the depressed *S-T* segment in a gradual ascent which develops no clearly recognizable wave and ends indeterminately about the *P* wave that follows (Figure IV, Lead II). In both types of record *U* waves are frequent. These abnormalities are most constantly seen in Lead II and have not been found (Case X excluded) except in association with a low serum potassium level.

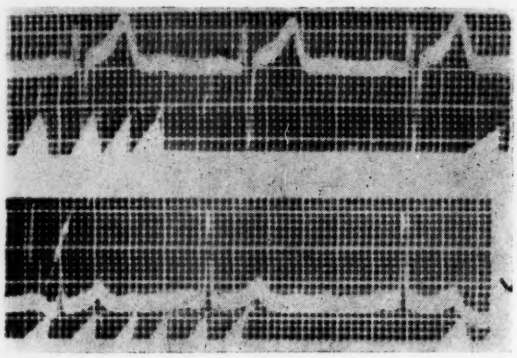

FIGURE IIIA.

Case IV. Before treatment. Electrocardiogram within normal limits.

Four patients have displayed irregularity of the pulse, and records are available of three of these. In Case II a *pulsus bigeminus* was found, but at the time when the electrocardiogram was taken the arrhythmia had disappeared. In other respects the tracings showed the changes that are considered to be distinctive of potassium deficiency (Figure IB). In Case I a tumultuous arrhythmia was present clinically indistinguishable from auricular fibrillation. The electrocardiogram showed the distinctive *ST-T* segment abnormality and the arrhythmia was found to be due to frequent premature ventricular and auricular systoles, many of the latter being blocked (Figure IV). In Case IV the patient died suddenly. An electrocardiogram taken twelve hours before death in this case revealed the ominous combination of a complex arrhythmia due to premature beats and the *ST-T* segment abnormalities which we consider to be diagnostic of grave potassium deficiency (Figure III).

In Case XI the patient also died suddenly, and in a tracing taken a few hours before death was found a coupling due to premature ventricular beats. The electrocardiogram showed the changes found in states of gross hypokalæmia, but autopsy revealed a small septal infarct.

With the exception of Case X noted above, the electrocardiographic abnormalities have been found in constant association with a low serum potassium level. The progress of the patients has shown a striking correlation between the electrocardiographic and biochemical findings. Furthermore, when muscular weakness has been present, the trend towards clinical improvement has been faithfully paralleled by the tracings. With recovery from the paresis the records return to normal.

For these reasons we consider that the electrocardiographic changes we have described are related directly or indirectly to the state of hypokalæmia. Furthermore, when the distinctive record is found, especially in association with arrhythmia, it is our opinion that the condition is a medical emergency, whatever the clinical status of the patient may appear to be.

Treatment and Prevention of Hypokalæmia.

Treatment of patients with hypokalæmia must be prompt and adequate. Sodium para-amino-salicylate therapy should be suspended immediately the condition is recognized. In Case VII death must be attributed to the continuation of therapy.

Cases III and VIII demonstrated that the condition is slowly reversible once sodium para-amino-salicylate therapy is suspended. In order to correct the electrolytic imbalance more rapidly, it is necessary to give large doses of potassium.

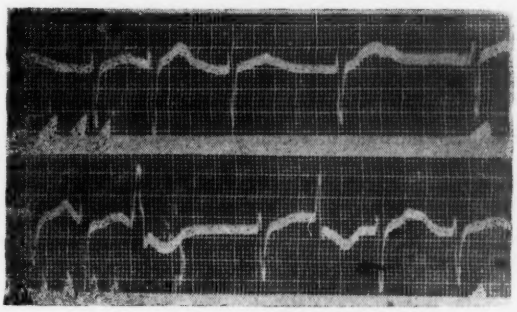

FIGURE IIIB.

Case IV. Serum potassium content 12 milligrammes *per centum*. Sinus arrhythmia in Lead V_4. Interpolated premature beat. *T* waves broad and flat. *Q-T* interval prolonged. Lead V_6, *T* waves broad. Complex arrhythmia with premature beats.

We have not found it possible to forecast the amount of potassium required in individual cases, and for this reason therapy is best controlled by daily electrocardiograms or serum potassium estimations. All patients have required large doses of potassium salts. When potassium chloride is used, 24 to 30 grammes of the salt are required every twenty-four hours until the serum potassium level or the electrocardiogram returns to normal.

The death in Case IV has led us to regard hypokalæmia with cardio-vascular abnormalities as a medical emergency, and if there is evidence of pronounced cardiac arrhythmia or enlargement, we consider that the intravenous use of potassium chloride is indicated.

In Case I it was found that without suspension of sodium para-amino-salicylate therapy, hyokalæmia could be controlled provided sufficient potassium chloride was administered. This has led us to the belief that hypokalæmia may be avoided by administering potassium concurrently with sodium para-amino-salicylate. We have insufficient experience to know how satisfactory such a régime will be, but we have used potassium para-amino-salicylate for this purpose and believe that it will prove safer than the sodium salt. However, it is obvious that this form of prophylaxis is merely replacement therapy and not treatment of the cause of the hypokalæmia itself.

Dosage and Preparations of Sodium Para-Amino-Salicylate Used.

In all cases sodium para-amino-salicylate was administered as the sodium salt, but doses were calculated as the acid. We found no definite relationship between the dose and the development of hypokalæmia. It occurred with a daily dosage of 15 grammes or 12 grammes. We found no unusual blood concentration of sodium para-amino-salicylate in patients developing hypokalæmia. Commercial preparations of sodium para-amino-salicylate vary considerably in purity (Bogen, 1950), but the material used by us was believed to be 95% pure and was obtained from two commercial sources. Traces of impurities were no doubt present, as the material was not white. These impurities have not been fully identified, but are at present being examined. Some of the material was obtained as the sodium salt, the remainder was converted to the sodium salt by the addition of sodium hydroxide to the acid, and the solution was flavoured with *Extractum Glycyrrhizæ Liquidum* (British Pharmacopœia) and used within a week of preparation.

Cause of Hypokalæmia.

The probable cause of hypokalæmia in the cases reviewed is either para-amino-salicylate itself or some impurity in the drug. Although we used sodium para-amino-salicylate exclusively, it is unlikely that the sodium radicle was

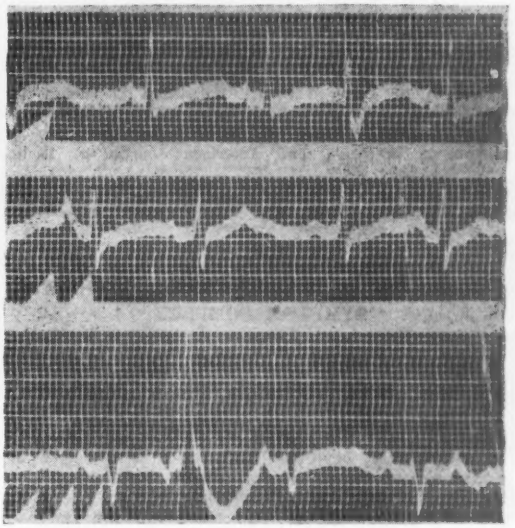

FIGURE IV.

Case I. Serum potassium level 11 milligrammes *per centum* on March 10, 1950, and 7·0 milligrammes *per centum* on March 11. Lead I, *S-T* depression with broad, flat *T* waves. One interpolated premature ventricular beat. Lead II, *S-T* depression, similar characteristic *ST-T* segment. *Q-T* interval prolonged. Lead III, *T* waves broad and flat. One premature ventricular systole.

responsible for the complication. Two contributory factors may be mentioned.

All patients suffered from active and extensive tuberculosis, and in some appetite was impaired; this may have led to a diminished potassium intake.

Further elucidation of the problem is required, and investigation of impurities contained in the drug and potassium balance studies are being undertaken to that end.

SUMMARY.

1. The development of hypokalæmia following sodium para-amino-salicylate therapy for tuberculosis has been described.

2. This complication was found in ten of sixty cases and was suspected in two others.

3. The main clinical features, muscular paresis and cardiac involvement, have been discussed, and the danger of the latter is stressed.

4. Treatment of hypokalæmia has been described. When the heart is seriously involved, the condition is considered to be a medical emergency.

5. Potassium para-amino-salicylate is considered to be safer than the sodium salt.

ACKNOWLEDGEMENTS.

We are considerably indebted to the staff of the Repatriation General Hospital, Heidelberg, who, by their cooperation, have made this study possible. We wish to thank Dr. A. H. Penington, Specialist in Tuberculosis, Repatriation Commission, and Professor R. D. Wright for their advice and helpful suggestions, and the chairman of the Repatriation Commission for permission to publish this paper. Our thanks are also due to Sister E. Hay and Miss L. Arnold for their electrocardiographic work, to Miss H. Wischusen for the photography and to Miss M. Mason for secretarial assistance.

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THE SURGICAL PATHOLOGY OF MÉNIÈRE'S SYMPTOM COMPLEX.[1]

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MÉNIÈRE'S SYNDROME or symptom complex is a term applied to a group of symptoms, the underlying ætiology of which is as yet unknown. In this condition the patient suffers from attacks of giddiness of the peripheral vestibular type, from deafness, often increasing, and usually from tinnitus.

Because the condition is not a killing disease, autopsy material for investigation and examination is scarce. However, in the last ten years eleven reports have been published (Lindsay, 1944) of examination of the inner ear at autopsy on patients who had suffered from Ménière's syndrome and who had died suddenly from some other cause, and the descriptions of the histopathological findings have been essentially the same in all cases.

Ménière in 1861 described a case in which a young girl suddenly became ill with vertigo, tinnitus, deafness and high fever. Death occurred two days later. At the post-mortem examination a diffuse hæmorrhage was found in the labyrinthine spaces. The actual ætiology in this case was undetermined. Alexander (1926) suggested from his studies on leuchæmia that this condition might have been present. Considerable confusion has existed as regards both classification and ætiology. It is now thought that the common group of symptoms known as Ménière's symptom complex is not the result of hæmorrhage into the labyrinth, but of a gross dilatation of the *scala media* of the cochlea and of the saccule and to a lesser extent of the utricle (Figures I to V). The membranous semicircular ducts do not appear to be affected on microscopic examination. There are atrophic changes in Corti's organ and in the spiral ganglion in the lower half of the basal turn of the cochlea; there are also, in some cases, changes of doubtful significance in the connective tissue around the *pars intermedia* of the endolymphatic sac; these changes will be described in detail later. Hallpike and Cairns (1938) think that the symptoms are due either to an increased production of endolymph or to an alteration in its physico-chemical constitution causing an increased osmotic pressure, with a consequent passage of water molecules from the perilymph into the endolymphatic space with dilatation of the latter—a condition often referred to as hydrops of the labyrinth.

In the past considerable difference of opinion has existed in regard to the ætiology of the disease and also as to the site or part of the vestibular or acoustic tract affected; different investigators have believed the part affected to be either the peripheral end organ (Crowe, 1938; Wright, 1940; Hallpike and Cairns, 1938; Furstenberg *et alii*, 1934, 1941; Brunner, 1939), the nerve itself (Dandy, 1934), the brain (Thornval, 1929; Skoog, 1939), or a central and peripheral combination (Grove, 1941).

Dandy at one time thought that only a lesion in the eighth nerve itself could cause Ménière's syndrome, since both hearing and equilibrium are affected. Later he thought that there was evidence that the central pathways were bilaterally involved (Crowe, 1938). He thought that a lesion in the end organ would be too diffuse not to be found. In the light of recent autopsy findings this hypothesis can be less easily sustained.

Thornval thought that nerve cells in the "otolithic centre" became gradually "charged" and when tension had reached a certain point, suddenly discharged, with the production of a Ménière's attack—an academic hypothesis without any basis in fact.

Grove, on the ground that tinnitus persists sometimes even after section of the eighth nerve, believed that changes (probably œdema) existed in both the end organ and the cochlear nuclei. There is no real justification for this assumption; the mechanism of the ætiology of tinnitus itself is unknown.

The Causation of the Symptoms.

There are a number of hypotheses as to the causation of the symptoms, and different *régimes* of treatment have been based on these.

Local Infection.

Some observers regard the condition as the result of a toxic infectious process in the labyrinth associated with an infected focus elsewhere in the body, and think that the disease begins as serous labyrinthitis (Wright, 1940, and Shambaugh, 1940). Dandy criticizes this, stating that if such were the case the condition would be commoner in childhood. The fact that no signs of inflammation are found at autopsy also makes this hypothesis unlikely.

Disturbed Water Metabolism.

Mygind and Dedering (1932) hold that there is abnormal water metabolism in the body, retention of fluid causing extracellular œdema. When this occurs in the labyrinth the endolabyrinthine pressure is raised.

There is as yet no proof of this. The support for the hypothesis rests on doubtful interpretation of success with therapeutic measures based upon it.

Allergy.

Those who support the allergic hypothesis believe that there is an increase in the permeability of the capillaries allowing extracellular œdema to occur. Animal experiments to prove this have not been convincing (Dean, 1939; Dohlman, 1939; Kobrak, 1927; Meyer, 1940; Atkinson, 1940).

Abnormal Sodium and Potassium Metabolism.

Furstenberg and his co-workers (1941) hold that there is a retention of sodium in the body, which is associated with a retention of water to maintain the osmotic balance. Blood level estimations have not confirmed this hypothesis.

[1] The subject matter of this paper provided the material for one of a series of lecture-demonstrations in pathology delivered under the auspices of the Melbourne Permanent Post-Graduate Committee to candidates for Part II of the Diploma of Laryngology and Otology in the University of Melbourne.

Talbott and Brown (1940) found an increased concentration of potassium in the serum during an attack.

Wolfson (1943) points out that disturbed water metabolism and abnormal sodium and potassium metabolism are interrelated, because any treatment which hopes to reduce the œdema must restrict both water intake and sodium *plus* potassium intake. There is a reciprocal arrangement between sodium and potassium in the body, in that an increase of sodium causes a decrease in potassium and *vice versa.*

A Vasomotor Disturbance.

More recently Atkinson (1946) has been an advocate of the hypothesis of a vasomotor disturbance. He points out that Lermoyez in 1919 described two groups of cases. Atkinson explains this division into two groups on the following lines. There are a number of elderly patients in their sixties or over who suffer from arteriosclerosis; he postulates that their attacks are due to a temporary vascular spasm, incited by a local degenerative fault, and causing a temporary anoxæmia of the labyrinth.

Then there is a younger age group, really a subgroup, whose symptoms may also be due to vascular spasm, which places them in a primary vasoconstrictor group; but the symptoms are possibly caused by some mechanism similar to that postulated by Lewis in Raynaud's disease. In both of these the vasoconstriction is temporary and is followed by vasodilatation. In a second smaller group the symptoms are due to primary vasodilatation, and these are mainly in the lower age group.

Atkinson separated these two groups, by means of the histamine skin test,[1] into a smaller "histamine-positive" group, giving an abnormally sensitive response to the test and comprising about one-sixth of all patients, and a larger group, giving a normal or negative response. The subjects in this latter group owe their symptoms to primary vasoconstriction. Their treatment consists in the ingestion of peripheral vasodilators, of which nicotinic acid is the most suitable for continued therapy.

Amyl nitrate, acetylcholine and histamine are suitable for relief of an acute attack. Vasoconstrictor drugs may precipitate an attack.

In the "histamine-positive", or second smaller and younger group mentioned above, the symptoms are due to vasodilatation, and vasodilator drugs tend to precipitate an attack.

Desensitization with histamine is the most effective treatment in this group, care being taken not to give too large a dose and so precipitate an attack. The rate of increase in dosage of histamine injection can be gauged to some extent by the degree of response to the test skin dose. Adrenaline, ephedrine and "Benzedrine" may be used to control an acute attack.

Atkinson correlated his hypothesis with the pathological findings (see later) in the following way. As by 1946 there had been eight other autopsy reports in undoubted cases of Ménière's disease besides the original three published by Hallpike and Cairns (1938), confirming the description given by these two authors of the characteristic pathological picture of dilatation of the membranous labyrinth, Atkinson accepts this.

[1] The technique of the histamine skin test is as follows. If 0·05 millilitre of 1 in 10,000 solution of histamine base (Abbott's Laboratories put out histamine diphosphate in ampoules of one millilitre of 1 in 10,000 solution calculated in terms of histamine base) is injected intradermally into the skin of the volar surface of the forearm two inches below the bend of the elbow, a weal develops, at first white, then yellow as serum transudes into it, then rapidly becoming surrounded by a zone of erythema. (i) If there appears after five minutes a weal one-quarter of an inch to one-third of an inch in diameter, with a surrounding flare of one and one-half inches to two and one-half inches in diameter lasting a further five to ten minutes, the response is "normal" or "negative". (ii) If at the end of five minutes a weal one-half an inch to three-quarters of an inch in diameter develops with a flare of one-half inch to two and one-half inches in diameter, and pseudopodia appear, sometimes one or two inches long or two shorter ones persisting for twenty to thirty minutes, the reaction is "positive". (iii) If smaller pseudopodia or buds appear, the response is "intermediate". In forty-eight hours or more a second test should be made and double the dose should be given intradermally. If still no pseudopodia develop, the response is regarded as "negative".

We still know very little for certain about the circulation of the endolymph. By analogy with the aqueous humour of the eye and with the cerebro-spinal fluid (both are fluids produced in closed systems and hence comparable), it is reasonable to suppose that the endolymph is a dialysate produced by the *stria vascularis*, and hence the quantity of endolymph will depend on variations in the blood flow in the capillaries of the stria. It is thought that the endolymph is absorbed in the *saccus endolymphaticus* (Guild, 1927).

In the primary vasodilator group, Atkinson explains the appearances in the following way:

> . Excess of endolymph represents local œdema from dilatation of capillaries and increased permeability of their walls. As this excess is formed and pressure increases, the function of the cochlea is damped down; hence the increasing deafness involving all tones, deafness which precedes the attack. This damping down affects, in the same way, the vestibule, decreases its sensitivity and puts it out of balance with its fellow on the other side until, eventually, the quantity of endolymph oversteps the capacity of the endolymphatic spaces, and Reissner's membrane ruptures at its weakest point, the helicotrema, with resulting vertigo. At the same time pressure in the cochlea is relieved with improvement in hearing. This the small histamine-sensitive group is the small Lermoyez group, *"le vertige qui fait entendre".*

This explanation appears to assume a repeated healing of the rupture at the helicotrema, of which we have no direct evidence.

It may be asked why these patients do not suffer giddiness as soon as one labyrinth becomes damped down, because of the over-activity of its fellow of the opposite side, and before Reissner's membrane ruptures at the helicotrema. Is it because the change is so gradual and compensation is possible? In a proportion of cases the damping-down is bilateral, but in many cases this is not so.

In the larger primary vasoconstrictor group, the mechanism of the attack differs but the histopathology is the same.

> The abruptness of the attack, with little or no warning, is due to a sudden diminution in blood supply from local vasospasm. This results in partial asphyxia of the labyrinth and consequent interference with the function of both vestibule and cochlea. The longer this asphyxia lasts, i.e., the more severe the degree of spasm the more severe is the disturbance and the greater is the immediate and residual impairment of function in both organs. But despite the functional difference in mechanism, the histological appearance will be the same as in the previous group, unless the patient should happen to die at the height of the attack. For when the spasm relaxes, it will be followed by an over-dilatation of the capillaries and a consequently increased production of endolymph, an œdema of the labyrinth. Just as the white numb fingers of the first stage of Raynaud's phenomenon are succeeded by the painful, blue and swollen fingers of the second stage.

This is by no means a proven hypothesis, but it is a possible explanation of the pathological findings on the basis of our present limited knowledge of the physiology of the labyrinth and the chemistry of its fluids.

Recently Atkinson (1949) has further elaborated his hypothesis that Ménière's syndrome is due to a disturbance of vascular function. From clinical experience in treatment he has formed the opinion that one factor, and perhaps the essential one, causing the symptoms is a vitamin deficiency. Further, he thinks that sufferers experience two types of vertigo, rotational and positional, and that these are associated with different and specific vitamin deficiencies. In rotational vertigo there is a sensation of rotation with nausea and vomiting; in positional vertigo there is lateral or vertical movement of objects and usually no vomiting.

The rotational-vertigo type patients show signs of nicotinic acid deficiency in the tongue, are in the histamine-insensitive group and are relieved by nicotinic acid.

Those who experience positional vertigo alone show signs of riboflavin deficiency in the tongue, eyes and skin, are histamine-sensitive and respond to the administration

of riboflavin alone. Those patients—and they are in the majority, Atkinson thinks—who experience both kinds of vertigo, show signs of deficiency of both nicotinic acid and riboflavin, give an immediate response to the histamine skin test, and are relieved by the exhibition of both these vitamin fractions. Atkinson also states that other symptoms common in patients with Ménière's syndrome can be related to other deficiencies; for example, fatigue irritability and palpitations are associated with thiamine deficiency and are relieved by its administration.

If these findings are confirmed, they will represent an important advance in the treatment of this debilitating malady.

The pressure in the labyrinth can be increased by an increased production of the endolymph, by decreased resorption or by alterations in its physico-chemical constitution. Hallpike and Cawthorne's view (1943) is that attacks of Ménière's syndrome are due to sudden asphyxia of the labyrinth. This occurs when there is a rapid rise in fluid pressure in the closed system of the membranous labyrinth, in response to a comparatively small increase in the volume of endolymph after the dilatation of the membranous labyrinth has reached practically the limits of its bony walls. This asphyxia would be relieved if Reissner's membrane, bulging through the helicotrema, ruptured, and the hearing would improve.

Pathological Findings.

The findings in the eleven autopsy cases published are fairly uniform. Almost always an extreme dilatation of the cochlear duct is present, and it often herniates through the helicotrema into the *scala tympani* (Figures I*b* and III). Reissner's membrane is a delicate structure, and with the dilatation of the cochlear duct it becomes bulged out into the *scala vestibuli*, and often, except at the helicotrema, is actually found pressed against its opposite bony wall (Figure III). At the helicotrema, where there is a dehiscence and the *scala vestibuli* and *scala tympani* join, Reissner's membrane, not meeting with any restraining wall at the gap, bulges through into the *scala tympani*.

The cochlear duct also bulges into the vestibule through the opening between the *scala vestibuli* and the bony vestibule. It is often dilated to such an extent that it covers the lower half of the stapes footplate, so displacing the saccule (Figure II).

The *ductus reuniens* and saccule are also greatly dilated. The dilatation of the utricle varies and is usually relatively less than that of the saccule; but when dilatation is gross, the utricle protrudes into the perilymphatic spaces of the semicircular canals at their ampullated ends (Figure V). Sometimes the saccule is found herniating into the inner extremity of the lateral semicircular canal.

No great distortion of the ampullated ends of the membranous semicircular ducts has been reported, and no dilatation of the ducts themselves. In other words, the degree of dilatation of the different parts of the membranous labyrinth varies; this is explained as due to differences in the thickness of the walls of these structures and to the differing degrees of fixation between the membranous labyrinth and the bony labyrinthine wall, but is not proven.

Atrophic changes are found in the neurosensory epithelium of the organ of Corti and most commonly in its basal turn. Complete disappearance of the organ of Corti has been found in the lower half of this turn (Altmann and Fowler, 1943).

An accompanying diminution in the number of ganglionic cells of and nerve fibres to the spiral ganglion in the lower half of the basal turn is usually found, and this is undoubtedly the result of ante-mortem pathological change (Figures I*a* and I*b*). However, great care must be exercised in interpreting histological sections, as it is difficult to exclude the possibility of post-mortem changes in this delicate end organ and to differentiate such changes from ante-mortem abnormality.

The maculæ and cristæ were normal or near normal in most of the eleven cases published, and any slight changes could not be said to be not due to post-mortem effects.

The endolymphatic duct is usually a little dilated in its proximal part, but otherwise its lumen is found to be within normal limits.

The presence or absence of the loose perisaccular connective tissue around the *pars intermedia* of the endolymphatic sac as described by Guild cannot be relied upon as a pathological finding, because this tissue is virtually absent or at least poorly developed in some normal subjects.

Guild (1927) showed by a Prussian-blue granule technique that the endolymph was absorbed through the wall of the *pars intermedia* of the *ductus endolymphaticus* into this loose perisaccular tissue. Wittmaack (1939) thinks some resorption of the endolymph also occurs by diffusion through Reissner's membrane into the *scala vestibuli*. Fibrosis of this loose perisaccular tissue has been found as well as absence and has been regarded as a possible contributory factor (Hallpike and Cairns, 1938); it has

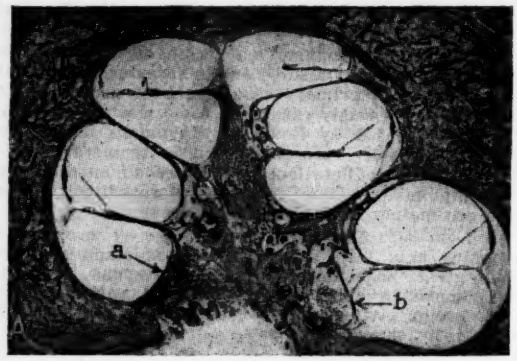

Figure Ia.

A horizontal mid-modiolar section through the right cochlea. The cochlear duct is normal and the loss of Reissner's membrane in the upper coil is an artefact. There is an extravasation of red cells at "*a*". The spiral ganglion of the basal coil shows degeneration ("*b*"). (After Lindsay, 1944)

been found in most of the eleven autopsy cases reported in the literature, but has also been found as a normal variation. Rollin (1940) states that the fibrosis either is due to local inflammatory change or is secondary to degenerative changes in the resorptive epithelium; but histologically there are no signs of inflammation, and the second possibility is mere conjecture.

The dilatation of the endolymphatic system is apparently due to increased endolymphatic pressure. There is no sign of any inflammation either in the perilymph or in the endolymph; thus the hypothesis that the condition may be akin to serous labyrinthitis is excluded. Other than this, the histo-pathological findings fail to give a clue to the actual reason why the changes in the membranous labyrinth occur, except that the cause would seem to lie within the endolymphatic system itself.

The dilatation may be due to over-production or diminished resorption of endolymph, or to the production of endolymph of an abnormally high ionic concentration, which would cause absorption of water molecules from the perilymph; or, lastly, a combination of these various factors may be present. Further, changes in the secretory activity of the *stria vascularis* or of any other areas which may secrete the endolymph are changes of function and will not necessarily appear as a gross morphological change at autopsy, and the absence of such changes cannot be taken as proof of functional normality.

The response to drug therapy may be interpreted as support for the hypothesis that Ménière's attacks of the type under discussion are the result of circulatory disturbances in the vessels of the labyrinth causing an increase in endolymphatic pressure, and further, that the mechanism was not the same in all cases; for example, in

some there was primary vasoconstriction followed by vasodilatation and in others primary capillary vasodilatation with increased permeability (Atkinson).

Lindsay (1942) does not agree that the attacks of giddiness are caused by the increased endolymphatic pressure acting directly on the sensory epithelium and causing asphyxia. He puts forward the hypothesis that the attacks of vertigo are caused by the herniation of the utricle into the semicircular canals, with subsequent distortion of the wall of the ampullæ interfering with the normal function of the cupula; this would explain both the attacks of giddiness and the depression of caloric excitability which is found in the later stages.

Lindsay maintains that the hearing loss is caused by the distortion of the sacculæ and of the membrane of Reissner, both of which may interfere with the sound transmission in the column of fluid in the cochlea. While this hypothesis may ultimately prove to be near the truth, there is no more proof of it than of any of the others.

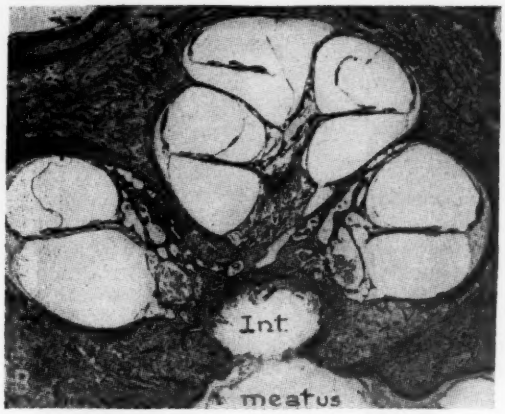

FIGURE Ib.

A vertical mid-modiolar section of the left cochlea. The cochlear duct is greatly dilated and beginning to herniate through the helicotrema. The spiral ganglion shows degenerative changes in the basal coil. (After Lindsay, 1944.)

The hearing loss in Ménière's syndrome takes the form of a fairly uniform slight to moderate involvement of the whole tone range, but with wide fluctuations in the threshold—that is, in the measurable level of hearing from day to day, especially in the lower and middle range, the upper and lower tone limits being fairly well preserved in the early stages. In the later stages the hearing loss is greater, especially in the upper tone range, and the fluctuations in the threshold decrease and finally disappear.

In the early cases these fluctuations would suggest that the hearing loss was probably due to reversible changes, and in fact in the early stages examination of Corti's organ reveals few, if any, histo-pathological changes.

As has been mentioned, Hallpike and Cairns hold that the acute attacks of vertigo are due to asphyxia of the vestibular end organs due to slight changes of endolymph pressure after the membranous labyrinth has become dilated to its fullest possible extent. The actual symptoms are due to over-action of the unaffected or less affected labyrinth. They maintain that in the interval periods, chronic depression of the function of the labyrinth is present because of partial asphyxia of the end organs from the increased endolabyrinthine pressure. These changes may be unilateral, but in the majority of cases are bilateral although varying in degree.

Pathology in Relation to Symptoms, Diagnosis and Treatment.

The diagnosis of Ménière's symptom complex rests upon the history of attacks of vertigo associated with loss of hearing of the perceptive type, which is variable at first, and usually with tinnitus. Apart from these findings the examination of the cranial nerves reveals no abnormal signs and cerebellar tests give normal results. There is no evidence of pyogenic disease of the middle or internal ear.

Brain (1938) has defined vertigo as "the consciousness of disordered orientation of the body in space".

The giddiness is obviously the most disturbing symptom to the patient. The attacks occur suddenly, although in some cases, possibly in the lower age histamine-positive group described earlier, a warning is given by the depression of hearing prior to the attack. Nevertheless, the actual onset of the giddiness is usually sudden, and it may occur while the patient is at rest or even asleep.

The sensation of rotation may be subjective, or objects may appear to rotate about the patient. However, not only may the dizziness take the rotatory form, but objects and the room itself may appear to move up or down or

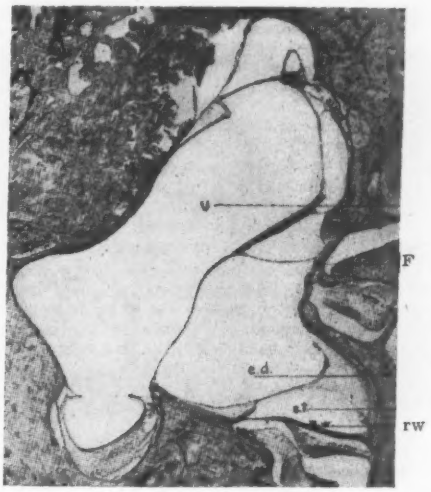

FIGURE II.

The cochlear duct at its lower end is greatly dilated and bulges into the vestibule, covering the lower half of the inner surface of the footplate of the stapes and displacing the saccule. The utricle is also dilated and the perilymphatic space reduced. *c.d.* = cochlear duct; *F* = footplate of stapes; *r.w.* = membrane of round window; *s.t.* = *scala tympani*; *U* = utricle. (After Altmann and Fowler, 1943.)

the patient may experience a "swimming feeling" in the head, a staggering sensation, a swaying sensation, and so on. Nystagmus may or may not be present during an attack.

The result of the caloric test varies, and one would expect the result during an attack to differ from that obtained in an interval period.

Crowe (1938) found in a series of 117 cases of Ménière's syndrome that the result of the caloric test was normal on both sides in 41, or 35%, subnormal only on the affected side in 22, or 19%, and absent on the affected side in 34 patients, or 29%. In the remainder for various reasons no vestibular tests were carried out. Also, in some cases in which the reaction was absent at one time, a subnormal positive result was obtained at another; this indicates that there is fluctuation in the pathological lesion in the labyrinth. Crowe's findings also indicate that the results of the caloric test are unreliable as diagnostic aids at least in Ménière's syndrome, but may help in the differential diagnosis. An absence of reaction to the caloric test should raise the suspicion of organic disease of the central nervous system—for example, an eighth nerve tumour.

The deafness is of the perceptive type, and in the early stages may vary considerably in degree and may be uni-

lateral or bilateral; if it is bilateral, it is usually of different degrees of severity on the two sides.

The tinnitus is usually high-pitched, but this also varies in different subjects; it may be bilateral, and is often more severe in the deafer ear. The cause of the tinnitus is not understood; it is thought to be of cochlear origin, but sometimes it persists after division of the eighth nerve.

Vertigo or at least dizziness is a symptom sometimes associated with a number of disease states—for example, hypertension and also hypotension (low blood pressure and anæmic states), in cardio-vascular disease, gall-bladder disease, *diabetes mellitus*, avitaminosis, organic heart disease and various disorders of the central nervous system and the eighth cranial nerve in particular, the most important of the last-mentioned being acoustic neuroma.

It is evident that the diagnosis should never be made without a thorough general physical examination. Furthermore, even though a condition is diagnosed by a process of exclusion as Ménière's syndrome, the diagnosis can never be conclusive because of our incomplete knowledge of the underlying pathology of the condition. A constant watch should be kept for the development of new symptoms or signs which might indicate the presence of a hitherto undiscovered organic lesion.

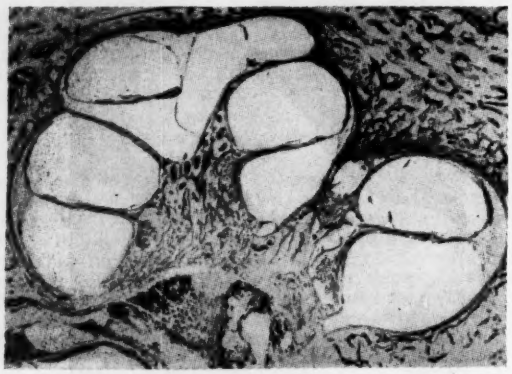

FIGURE III.

Showing gross dilatation of the *scala media* (cochlear duct) with displacement of Reissner's membrane on to the wall of the *scala vestibuli*, and herniation into the *scala tympani* at the helicotrema. (After Hallpike and Cairns, 1938.)

With regard to prognosis, it sometimes so happens in cases of unilateral deafness and tinnitus with vertigo that the function of the cochlea and static labyrinth is virtually lost, the opposing unaffected labyrinth compensates and the attacks of giddiness cease. There is almost complete or complete deafness on the affected side and the tinnitus usually disappears. Although this means that the disease is cured so far as that ear is concerned, it is a heavy price to pay.

It may be said that, despite the lack of knowledge of the ætiology of Ménière's syndrome, treatment, whether it is described as palliative or as empirical, can arrest the course of the disease in many cases and keep it under control for long periods in some and apparently completely effect a cure in others.

The actual details of the various drugs and methods of treatment may be obtained from the standard text-books, but certain principles may be profitably discussed here; some have already been referred to in the section on ætiology. It has often been stated that no form of medical treatment has any particular advantage over the others, and that as remissions in the symptoms are characteristic of the condition, one has to be particularly careful in assessing the results of any form of treatment.

The rationale of a number of forms of treatment which have been found useful is as follows. (*a*) General tonic treatment, promotion of measures to restore good general health. (*b*) Sedative treatment, including the use of barbiturates and bromides. (*c*) Other drug treatment, the use of hyoscine (on analogy with its use in seasickness), the use of the atropine group of drugs (the anti-spasmodics). (*d*) The restriction of sodium (common salt) intake in the diet (Furstenberg *et alii*, 1941) and the restriction of the fluid intake (these measures are complementary to some extent and it is hoped by their use to make hydrops of the membranous labyrinth less likely). (*e*) The ingestion of an increased quantity of potassium in the form of potassium chloride, in combination with a modified sodium-free diet (Talbott and Brown's treatment, 1940). (*f*) The use of vasodilator and vasoconstrictor drugs according to whether the subjects are histamine-insensitive or not (Atkinson, 1946; Sheldon and Horton, 1940). The drugs used also vary in potency according to whether they are used in an acute attack or not. (*g*) Surgical treatment. This is not used unless medical treatment has failed because the function of the cochlea and static labyrinth on that side is destroyed; hence surgical methods are most suited to unilateral cases.

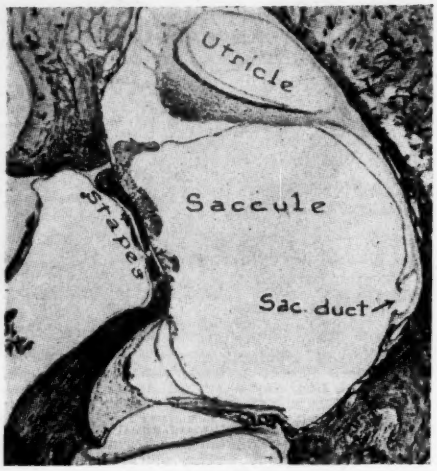

FIGURE IV.

Section through left vestibule, showing the utricle and dilated saccule with obliteration of the perilymphatic space. (After Lindsay, 1944.)

Dandy's operation entails division of the eighth nerve or at least its vestibular division—quite a formidable undertaking.

Another type of surgical cure consists in the destruction of the labyrinth either by labyrinthectomy or by injection of alcohol into the lateral semicircular canal, or the destruction of the membranous labyrinth through the lateral canal by diathermy cautery.

Passe (Passe and Seymour, 1948) has surgically interrupted the sympathetic nervous system in the neck on the affected side in unilateral cases, and on the worse affected side in bilateral cases. He removes the superior cervical sympathetic ganglion, divides the preganglionic fibres of the first and second thoracic segments, and strips the sympathetic fibres from the first part of the vertebral artery and divides it. This method is designed to relieve the group whose symptoms might be attributable to primary vasoconstriction. It is carried out in the treatment of subjects who have failed to respond to conservative measures, in the author's experience a very small group. The series of patients operated upon (12 in number) is small, and Passe's paper is in the nature of a preliminary report. Vertigo was relieved in all but one case; tinnitus was relieved completely in three cases and partly in others. Improvement of hearing was also claimed in all but two cases, though it is admitted that if the nerve deafness is severe it is beyond relief.

Recently Fowler (1948) has reported the use of streptomycin in the treatment of Ménière's syndrome. Damage to the labyrinth is not infrequent after large doses of this drug. A recent study (Barr *et alii*, 1949) showed that a daily dose of less than one gramme and a total dose of less than 60 grammes carry a relatively small risk of vestibular damage provided there is no impairment of renal function. The evidence that streptomycin may affect the hearing is as yet less conclusive, because in most cases in which deafness occurred in the study mentioned above, the disease for which the drug was given may have caused the damage to the acoustic division of the eighth nerve; but it appears that the drug may damage the hearing. The question of where the vestibular nerve is damaged is still not settled.

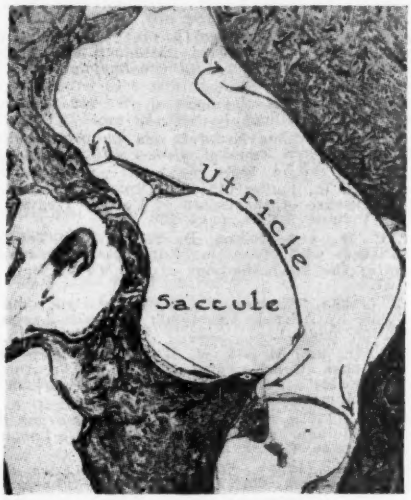

FIGURE V.

Section through the left vestibule posterior to that in Figure IV, showing the dilated utricle and saccule and almost complete obliteration of the perilymphatic space. The utricle is herniated at the ampulla of the posterior semicircular canal (lower arrows) and at the ampullæ of the superior and horizontal canals (upper arrows). (After Lindsay, 1944.)

In 1947 Glorig and Fowler, from clinical studies, thought that the nerve was impaired peripherally. In 1949 Floberg, Hamberger and Hyden, using cytochemical methods experimentally on animals, found that there was injury both in the vestibular ganglion peripherally and in Deiter's nucleus centrally.

Fowler has used streptomycin as a specific neurotoxin to damage the vestibular organ in cases of vertigo which would not respond to other forms of treatment. It is a rather drastic form of treatment, and in the dosage used the streptomycin produced what amounted to bilateral physiological vestibular nerve section.

Fowler states that the method should be limited to patients under the age of fifty years with Ménière's symptom complex affecting both labyrinths, for which medical treatment has been tried and has failed. If only one labyrinth is affected and medical treatment fails, obviously destruction of that labyrinth is the method of choice. In Fowler's first four experimental cases the attacks of vertigo were completely stopped for periods ranging from five to nine months, and in three of the four the hearing was unaffected. However, the patients lost all reaction to labyrinthine stimulation, and if the function of the labyrinths was not greatly impaired by the Ménière's syndrome, the immediate effect of the streptomycin was severe vertigo. The older the patient, the less perfect was the compensation which took place; in any case it was never complete, as all patients had difficulty in walking in the dark. The action of the streptomycin is apparently to some extent selective, in that the vestibular function can be affected without harm to the cochlear function. However, it would be applicable to only a small percentage of cases, even if further trial established its use as a worthwhile measure.

Summary.

Ménière's syndrome or symptom complex is a term applied to a group of symptoms of as yet unknown ætiology. It is characterized by attacks of vertigo of the peripheral vestibular type, deafness and tinnitus.

In the last ten years eleven reliable reports of examinations of the inner ear at autopsy on patients who had suffered from Ménière's syndrome have been published with similar findings.

In Ménière's original case described in 1861, a diffuse hæmorrhage was found in the labyrinth, possibly due to leuchæmia. The pathological findings in the class of case now grouped as Ménière's syndrome are very different. In these there is gross dilatation of the *scala media* of the cochlea, of the saccule and to a lesser extent of the utricle. Microscopic examination reveals no damage to the membranous semicircular ducts. There are atrophic changes in Corti's organ and in the spiral ganglion in the lower half of the basal turn of the cochlea, and certain changes of doubtful significance in the connective tissue around the endolymphatic sac.

The symptoms are possibly due either to an increased production of endolymph, or to an alteration in its physicochemical constitution causing increased osmotic pressure; either will cause dilatation of the endolymphatic space, and the condition has been called hydrops of the labyrinth.

Considerable difference of opinion has existed and still exists about the ætiology. Different schools have believed the part affected to be the peripheral end organ, the nerve itself, the brain, or a central and a peripheral combination. The arguments for and against these views are discussed.

The principal hypotheses as to the cause of the symptoms are as follows:

1. That there is a toxic infective process in the labyrinth associated with an infected focus elsewhere in the body, and hence that the disease is mild serous labyrinthitis. There is no microscopic evidence of this.

2. That there is abnormal water metabolism in the body, retention of fluid causing hydrops of the labyrinth. There is no proof of this, but there is some clinical backing based on treatment directed toward restriction of fluid intake.

3. That allergy causes an increased permeability of the capillaries of the *stria vascularis*. Animal experiments to prove this have not been convincing.

4. That there is abnormal sodium and potassium metabolism in the body. Treatment by restriction of sodium intake is linked with restriction of fluid intake.

5. That the condition is due to a vasomotor imbalance. Atkinson separates the cases on this basis into the primary vasoconstrictor group and a smaller group in which the symptoms are caused by a primary vasodilatation.

The autopsy findings are the same unless death occurs at the height of an attack, because vasodilatation follows the primary vasoconstriction. Atkinson separates the cases clinically according to whether they are sensitive or insensitive (the larger primary vasoconstrictor group) to histamine, and he arranges his treatment accordingly, giving vasodilators to the members of the primary vasoconstrictor group and desensitizing the members of the primary vasodilator group with histamine.

The morphological findings are described in detail, and the interpretations of these by well-known workers are given, notably those of Hallpike and Cairns, of Atkinson, and of Lindsay.

The pathology in relation to symptoms, diagnosis, prognosis and treatment is then discussed. The type of giddiness, the varying results of the caloric test, the varying effect on the hearing and the tinnitus at different stages are dealt with.

Because vertigo is a symptom associated with many disease states, the diagnosis of Ménière's syndrome should never be made without a thorough general physical exami-

nation. Furthermore, even though a condition is diagnosed by a process of exclusion as Ménière's syndrome, the diagnosis can never be conclusive because of our incomplete knowledge of the underlying pathology. A constant watch should be kept for the development of new signs or symptoms which may indicate the presence of a hitherto undiscovered organic lesion of the type, for example, of an acoustic neuroma.

Despite the lack of knowledge of the ætiology, medical treatment, whether described as palliative or as empirical, can arrest the course of the disease in many cases and keep it under control for long periods in others, and in some it can apparently effect a complete cure.

The rationale of various treatments, medical and surgical, is briefly discussed.

With regard to prognosis, it may happen that in unilateral cases the function of both the cochlea and the static labyrinth is virtually lost, the opposing unaffected labyrinth compensates and the attacks of giddiness cease, hearing is lost and the tinnitus usually disappears. Although the disease is cured as far as that ear is concerned, it is a heavy price to pay and one to be feared in bilateral cases.

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TREATMENT OF SYPHILIS WITH PENICILLIN AT THE GOVERNMENT VENEREAL DISEASES CLINIC, SYDNEY: PRELIMINARY REPORT.

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Although penicillin had been used at the Department of Public Health clinic for many years for the treatment of gonorrhœa, it was not until the introduction of procaine penicillin that it was considered practicable to give treatment for syphilis as an out-patient procedure.

It was decided to use penicillin unsupported by arsenic or heavy metal for the treatment of primary and secondary syphilis, but to give a short preliminary course of bismuth in the tertiary, late and latent infections.

In all cases a positive diagnosis was made either by dark-field examination or by blood tests, or by both methods; the results of blood tests were always confirmed by a subsequent test. A few of the early patients received procaine penicillin in oil, but when procaine penicillin combined with aluminium monostearate became available, this preparation was used exclusively.

In order to standardize the treatment as much as possible, I drew up the following schedule for the treatment, retreatment and surveillance of the group of patients under investigation.

I. Schedule for treating primary and secondary infections.

Start the course with a single injection of 0·3 mega units of penicillin. Follow this with a single injection of 0·6 mega units on each of the succeeding nine days (excluding Saturday and Sunday). The patient will thus receive 5·7 mega units of penicillin.

Blood tests are to be done before and at 3 or 4 day intervals during the treatment period, a titration being done on all positive bloods. If the titre is high in the original test and does not fall or if the titre, low originally, rises rapidly and remains high during the course of treatment, continue the daily injections for a further 5 days. The patient will thus receive a total of 8·7 mega units of penicillin.

The blood is to be tested again two or three days after completion of the penicillin course and then at monthly intervals for 12 months. If after 12 months the blood tests are satisfactory (i.e. the blood has been negative for 6 months or more), the surveillance periods can be extended to 3 months. In all cases the monthly blood tests must be continued until the patient has been sero-negative for 6 months. In normal cases an examination of the cerebro-spinal fluid should be made at the end of twelve months or sooner if a sero-relapse occurs or the blood titre rises after an initial fall.

Re-treatment is indicated:

1. If clinical relapse occurs (often difficult to differentiate from re-infection).

This may take the form of:

(a) An ulcer on the penis, not necessarily at the site of the original lesion, with or without inguinal adenitis, giving a positive dark field test. Blood may be negative.

(b) Secondary lesions of skin, mouth or anus.

(c) An ulcer on the penis, with or without inguinal adenitis, which gives a negative dark field test, but is accompanied by a sero relapse in a blood that has been negative.

A penile lesion, which is dark field negative on several occasions and which ultimately heals, in a patient who is sero negative, must not be ignored. The blood should be tested at short and regular intervals for three months to exclude the possibility of relapse or re-infection. Sulphadiazine or sulphathiazole should be given in doses of 8 tablets daily (in 4 doses of 2 tablets) for four or five days. This frequently helps as a "therapeutic test", non-syphilitic sores usually responding rapidly while syphilitic lesions are unaffected.

2. If serological relapse occurs.

This must be established by several blood tests performed over a variable period, depending on when the possible relapse occurs.

(a) In an original sero negative case if the "relapse" occurs one or two months after completion of treatment, a period of 2 or 3 months could be allowed for checking purposes. If, on the other hand, the "relapse" occurs 6 months or longer after completion of treatment, checking of the positive blood should be completed in 3 or 4 weeks.

(b) In original sero positive primary or secondary cases the blood titre may rise and fall slightly, but will usually become negative after some months.

A relapse is to be suspected if, after returning to negative for 3 or 4 months, the blood test reverts to positive. This reversal of the blood test should be checked, as indicated above, over a long or short period according to the time at which the "relapse" occurs. In general the later the "relapse" occurs the less time should be wasted upon checking before re-treatment is commenced.

3. In original sero positive or secondary cases.

(a) If the blood is positive in low titre for 9 months or in high titre for 6 months, showing no sign of becoming negative.

(b) If the blood originally in low titre shows a rising titre over a period of six months, or four months if the rise is abrupt or very high.

(c) If the blood originally of high titre shows an initial fall, but does not become negative at the end of twelve months.

(d) If the blood originally of high titre shows an initial fall and remains positive in low titre for a time, then rises. The rise in titre should be checked on two or three occasions over a period of four weeks before re-treatment is commenced.

II. Schedule for the treatment of late infections.

Commence with a short course of bismuth—say one a week for 10 weeks—and follow with the penicillin course. Starting with 0·3 mega units and continuing with 0·6 mega units daily for 14 consecutive days (excluding Saturdays and Sundays).

As in early cases the blood is to be tested before, during and after the penicillin course. A reversal of a positive test to a negative is to be hoped for but not expected, a large proportion of these cases remaining positive in spite of any treatment. If the blood previously positive in high titre, reverts to a positive in low titre, or if previously positive in low titre continues as such, it is the most that can be expected in many cases.

The cerebro-spinal fluid should be examined at six months and again at 18 months. It frequently takes 18 months for all tests to become negative in the cerebro-spinal fluid.

When it was decided to use penicillin for the treatment of syphilis it was realized that special efforts should be made to keep the patients receiving penicillin therapy under control.

Normally all cards of patients attending the syphilis clinic are checked every two weeks and a letter is sent to defaulters. If this first letter fails to bring about the patient's reattendance or a satisfactory explanation for his failure to attend, a second letter is sent warning him of possible legal proceedings for default. If this second letter fails, prosecution is usually proceeded with.

This procedure was considered insufficient in the special case of this group of patients under review. The following plan was adopted. Patients receiving penicillin therapy must attend between the hours of 9 a.m. and 2.30 p.m. during the treatment period, and thereafter on the date set down on their card by the medical officer. The patient's cards were checked each day, and any man who during the treatment period failed to attend by 3.30 p.m. was written to on the same day. Those under surveillance who did not attend on the appointed date were written to on the following day.

All this was explained and the patient's verbal guarantee to cooperate was obtained before treatment was started.

This investigation was commenced on May 27, 1949, and up to the present time (June 2, 1950) 182 patients have been treated. These can be divided into the following groups: (i) early syphilis; these patients are 118 in number; of them 23 had already received some arsenic and bismuth therapy; (ii) late and latent infections; these patients number 57; 42 of them had already received some treatment with arsenic and bismuth or bismuth alone before starting on the penicillin course; (iii) relapses of previous early infections; these patients number seven; two of them had had some treatment since their relapse, but before the penicillin therapy.

It is too early to give findings in terms of "successes" and "failures", but I think the results to date are both interesting and encouraging.

Each patient's serological reactions were set out graphically; thus comparisons were facilitated and it was made possible to see at a glance whether progress was satisfactory or not.

In the groups of patients who had already received some treatment before commencing the penicillin therapy, it is difficult to assess results, as many may have been cured or well on the way to cure before the penicillin was given. It is also too early to make any statement about the effect of penicillin on the late and latent infections. There remains, then, a group of 95 patients with untreated early infections (31 with primary infections who were "sero-negative", 64 with primary and secondary infections who

were "sero-positive") and a small group of five patients with relapsed early infections who had received no treatment since their relapse.

In order to simplify the study of the individual patient's serological reactions and to make possible a quick comparison of the serological reactions of many patients, some form of linear recording of results was necessary. A scheme of numerals and signs was adopted, the tests made before, during and after treatment being separated by commas. The statement below is self-explanatory:

x = monthly test omitted.
0 = Wassermann test, negative response.
½ = trace of positive response.
1 = weakly positive response.
2 = positive response in a dilution of 1 in 5.
3 = positive response in a dilution of 1 in 10.
4 = positive response in a dilution of 1 in 20.
5 = positive response in a dilution of 1 in 40.
6 = positive response in a dilution of 1 in 80.
7 = positive response in a dilution of 1 in 160.
8 = positive response in a dilution of 1 in 320.
+ = positive result, but no titration test made.
( ) = two or more tests made in the same month.
— = first post-treatment test omitted.

By the use of this form of recording results, patients' serological progress can be readily appreciated and easily set out in graph form. For example, the record of a patient with typical "sero positive" primary syphilis is "6,557, –3110000000" (Case 5), and that of a patient with typical secondary syphilis is "4,565, –33½0000000" (Case 8).

The five patients who had relapsed are of interest because they had all been previously treated with penicillin. Details of their original infections and relapses are shown in Table I. Their serological progress is shown below: Case 24: 0, 0 ½ ½, –000000 (six months' surveillance); Case 100: 4, 6767, –443 (three months' surveillance); Case 123: 3, 3+3, +10 (two months' surveillance); Case 124: 3, 2+2, ½ ½ (two months' surveillance); Case 173: 5,56575,6 (course just completed).

Our own relapse cases (Cases, 3, 11 and 31) give interesting pictures. Case 3 may be summarized as follows: 0x,331,xx $\underset{\text{first relapse}}{\overset{3,43+3,}{\text{———}}}$ –000 $\underset{\text{second relapse}}{\overset{4,4+334}{\text{———}}}$ –1000 (both relapses were infectious and serological). Case 11 may be summarized as follows: 3,323,–110 $\underset{\text{relapse}}{\overset{(531)\,(333)\,(56)}{\text{———}}}$, +5 under treatment. When a relapse appeared imminent the blood was tested at frequent intervals. The fall to an "incomplete positive" result on the third test made one hope that there had been only a temporary rise in titre, and a month was allowed to elapse before the next test was made. The last five tests were made over a period of two months. Case 31 may be summarized as follows: 6,776,–x $\underset{\text{relapse}}{\overset{255\,(46)\,(56)}{\text{———}}}$ retreatment commenced. These three patients had received 5·7, 7·5 and 5·7 mega units respectively.

"Sero-Negative" Primary Cases.

The so-called "sero-negative" primary cases were not all, strictly speaking, "sero-negative", as in six a "trace of positive" result and in five a "weak positive" result were obtained to tests performed immediately before treatment, but they are included in this group for convenience. The group consisted of 31 patients. Three were seamen and left the State before completing their treatment, and three others have just completed their course.

Of the 25 patients who have completed their courses and have been under observation for periods varying from one to eleven months, two were not "sero-negative" after one month, but they yielded only a "trace of positive" result. One of these is now "sero-negative", while the other (Case 134) has been under surveillance for only one month. The remaining 23 patients have yielded consistently negative serum findings for their periods of observation, as listed below: eleven months, two patients; ten months, one patient; eight months, one patient; six months, four patients; five months, four patients; three months, three patients; two months, five patients; one month, three patients. Twenty-two patients had three or more tests performed during their course of treatment; 12 showed some increase in positivity above the original test result, seven in all three tests, three in two tests and two in one only. The increase was usually slight (from a "negative" to a "trace of positive" or a "weak positive", or from a "trace of positive" to a "weak positive"). On only two occasions was there a rise to a full positive result. The serological records of these two patients are as follows: Case 115: 1,411,½00; Case 134: 1,+4+,3½. One patient did not return for a month after completing his course, but in all the other cases the test result had fallen (usually to negative) by the time the first post-treatment test was made.

Of the 31 patients who had had one test or more performed during their course, 13 showed an increase in positivity in the result of the first test (that is, three or four days after the commencement of treatment when they had received 0·9 or 1·5 mega units of penicillin).

From the foregoing it seems unlikely that the usual dose (0·3 mega unit) of penicillin used in the treatment of gonorrhœa would in any way delay the serological reaction in a patient incubating syphilis. On the contrary, the serological rise followed by the rapid fall immediately after the penicillin injections had been completed suggests the possibility of a provocative action.

In the presence of a primary lesion, however, even as small a dose of penicillin as 0·3 mega unit may interfere with the dark-field examination.

"Sero-Positive" Primary and Secondary Syphilis.

The next group of 64 patients is made up of 45 who had "sero-positive" primary infections and 19 who had secon-

Table I.

Case Number	Original Infection. Type.	Original Infection. Treatment.[1]	Period when Relapse Occurred.	Relapse. Type.	Relapse. Treatment.[1]
24	"Sero-negative"; primary syphilis.	P.A.M., 9·0. A., 2. B., 2.	Three months.	Infectious ("Sero-negative").	P.A.M., 9·0.
100	Secondary syphilis.	P., 4·0. B., 25.	Two and a half years.	Serological.	P.A.M., 8·7.
123	Secondary syphilis.	P.O.B., 3·0. A., 7. B., 8.	One year seven months.	Serological.	P.A.M., 5·7.
124	"Sero-positive"; primary syphilis.	P., 6·0. Ac., 29.	Eleven months.	Serological.	P.A.M., 5·7.
173	"Sero-negative"; primary syphilis.	P.O.B., 3·0. A., 16. B., 24.	Three years.	Serological.	P.A.M., 8·7.

[1] "P.A.M." = procaine penicillin with aluminium monosterate (mega units); "P.O.B." = penicillin in oil and wax (mega units); "P." = soluble penicillin (mega units); "B." = bismuth (number of injections); "A." = arsenic (number of injections); "Ac." = "Acetylarsan" (millilitres).

TABLE II.
"Sero-positive" Primary and Secondary Syphilis.

Period at which Results Recorded.	Total Number of Cases.	"Positive" Response.	"Weak Positive" Response.	"Trace of Positive" Response. (a).	"Negative" Response. (b).	Total (a) plus (b).	Relapses.
1 month	45	27	7	6	5	11	
2 months	42	16	8	6	12	18	1 (Case 3)
3 months	33	8	8	4	13	17	1 (Case 31)
4 months	30	2	5	4	19	23	1 (Case 11)
5 months	23	2	2	1	18	19	
6 months	18	—	3	2	13	15	
7 months	15	—	—	3	12	15	
8 months	12	—	1	—	11	11	
9 months	6	—	—	1	5	6	
10 months	4	—	—	—	4	4	
11 months	3	—	—	—	3	3	

dary infections. Of these 64 patients, 50 have been under observation for periods ranging from one to eleven months. Six have just completed their treatment course and eight have been lost from observation. This last group of eight patients consisted of the following: (i) two defaulters, each of whom had completed his treatment course; (ii) four patients who had left the State, all except one of whom had completed their treatment, two having also had their first post-treatment blood test; (iii) two patients who had been transferred to country practitioners, but not before completing their course, one having also had his first post-treatment test.

The 50 patients who have remained under observation have been almost unbelievably regular in their monthly attendances. On only 12 occasions has a month been missed, which is equivalent to approximately once to every 24 attendances. As most of these patients who miss appointments are seamen, who are often unable to be in port at the correct time, the attendance rate is even better than appears at first sight. Actually only five patients (excluding the two defaulters) have missed appointments. However, this failure to attend each month, and the fact that on four occasions blood tests gave an anti-complementary result, are responsible for the apparent discrepancy between the total number of patients under observation and the figures in Table II, which shows the serological results at various months from one to eleven. The tendency towards "sero-negativity" is apparent in this table. It can be seen that the proportion of "sero-positive" patients decreases each month, falling from 27 out of 45 in the first month (which in itself is a considerable fall in one month) to 16 out of 42 in the second month and eight out of 33 in the third month of observation.

This tendency to "sero-negativity" is shown again in a study of the serological charts of 28 patients who had been under surveillance for four months or longer, and from whose records it was possible to compare the results of tests at one month and four months. Of these 28 cases, the reading at the fourth month was less than that at the first in 26, equal to it in one and higher than it in one —this last case being one of the relapses (Case 11). The two other patients with relapses could not be included in the above group, as they had both failed to attend for their first monthly blood test. It seems also that one should expect the blood test result to become negative, or almost negative, by seven months.

The decrease in positivity varied a good deal, but was usually fairly rapid. Among 30 patients who were observed for four months or longer, the rate was slow in three cases, gradual in eight cases, rapid in eight cases, and very rapid in 11 cases.

Eight patients' serological records are shown in Table III, to illustrate the fall in positivity. A study of the serological charts of the group of patients under review revealed a further point—namely, that a high titre in the pre-treatment and treatment tests did not necessarily mean that the reversal to negative would be slow. This is illustrated in Case 41, that of a "sero-positive" primary infection, the summarized findings in which are as follows: 7,855,5311$\frac{1}{2}$00. On the other hand, another patient (Case 102), who has been under surveillance for only three months, does not appear to be progressing very satisfactorily. His serological record is as follows: 6,+87,7+56.

TABLE III.
Rate of Decrease in Positivity.

Rate.	Case Number.	Primary or Secondary Syphilis.	Dose. (Mega Units.)	Serological Chart.
Slow ..	1	Primary.	5·7	5,556,5441121000000
	43	Secondary.	5·7	+,7+7, 5+ +421$\frac{1}{2}$
Gradual ..	30	Secondary.	5·7	5,77, −533$\frac{1}{2}$0
	16	Primary.	5·7	6,656, −45311$\frac{1}{2}\frac{1}{2}$0
Rapid ..	29	Primary.	5·7	3,64,321$\frac{1}{2}\frac{1}{2}$000
	41	Primary.	5·7	7,855,5311$\frac{1}{2}$00
Very rapid ..	12	Primary.	5·7	4,555,5$\frac{1}{2}\frac{1}{2}$00000
	23	Primary.	6·3	7,664,3$\frac{1}{2}\frac{1}{2}$0000

This man, however, may not be suffering from a "sero-positive" primary infection. He had syphilis in 1920 and was treated with "606" and apparently cured. He attended the clinic in 1937, having positive blood findings, and was treated till 1941. His blood tests gave negative results between 1940 and 1943. On January 12, 1950, he again appeared at the clinic with an ulcer on the penis, which had been present for one day and had occurred four weeks after exposure with a prostitute. Dark-field examination gave negative results on four occasions; but although both the Wassermann test and Kahn's test produced negative results on January 16, the blood test yielded a positive reaction with a dilution of one in five on January 31 and another positive reaction with a dilution of one in 80 on February 6.

Another point of interest is that of 50 patients who had a quantitative pre-treatment test and one or more quantitative tests during the treatment course, 26 showed an increase in titre at one or more of the tests during treat-

ment above that of the pre-treatment tests. On 21 occasions the increase was found at the first test. This latter figure approximates closely to that found in the "sero-negative" group of patients. As was mentioned earlier, all patients' blood was tested, as a routine measure, immediately before the penicillin course. In 57 of the 64 "sero-positive" and secondary cases a quantitative test was performed. It might have been expected that the secondary infections would produce a preponderance of high titre readings, but this does not appear to be the case. The results are shown in Table IV.

TABLE IV.

Degree of Positivity at Start of Course.

Dilution with which Result Positive.	Number of Patients.		Total.
	Primary Syphilis.	Secondary Syphilis.	
1 in 10	3	1	4
1 in 20	7	6	13
1 in 40	10	4	14
1 in 80	11	7	18
1 in 160	5	0	5
1 in 320	3	0	3
Totals	39	18	57
No titration	6	1	7

Penicillin Reactions.

Seven (3·8%) of the 182 patients had an allergic reaction to the procaine penicillin. This took the form of urticaria (usually fairly generalized) and, on all except one occasion, angioneurotic œdema. The œdema was severe and was usually confined to the hands and feet, but occasionally the legs and forearms were also affected. In one case even the knees and thighs became œdematous. These reactions appeared to be unaffected by the use of "Benadryl", but subsided usually in from five days to a week. They occurred in two cases fourteen days from the commencement of the penicillin therapy, and in one case each on the following days: ninth, twelfth, thirteenth, fifteenth and eighteenth. This is later than the usually stated time for such reactions, which is given as ten days.

Conclusion.

In conclusion, it is worth reporting that of the 182 patients treated only three defaulted and remained in default, and none before completion of their courses of treatment. This is a very low figure (1·6%) and we like to think that our "pre-treatment pep talk" is responsible for it.

Summary.

1. Schedules for procaine penicillin therapy in syphilis and indications for retreatment are presented.

2. The importance of control and follow-up investigation of patients receiving penicillin therapy is stressed, and the method adopted at the New South Wales State Government venereal diseases clinic is described.

3. Of 75 patients with early syphilis who have been under observation for periods of from one to eleven months, three have relapsed. The remainder appear to be progressing satisfactorily. Of 182 patients who had received procaine penicillin courses, seven (3·8%) had allergic reactions.

4. The value of quantitative blood tests is indicated and a useful linear method of recording patients' serological progress is illustrated.

Reports of Cases.

BARBITURATE IDIOSYNCRASY FOLLOWING LUMBAR PUNCTURE: A CASE REPORT.

By V. S. HOWARTH,

Gordon Craig Fellow in Urology, The University of Sydney, and Royal Prince Alfred Hospital, Sydney.

UNDUE SENSITIVITY to barbiturate drugs is a well-known phenomenon. R. J. McNeill Love records having performed lumbar puncture for this condition on the advice of Sir William Willcox. The rationale of the procedure given by this author is that cerebro-spinal fluid is withdrawn which contains a considerable amount of the narcotic, which is then replaced by a fresh fluid of lower narcotic content. Whether or not this is a correct explanation of the beneficial effects observed is doubtful; but that the operation is effective is undoubted. Hamilton Bailey records the value of lumbar puncture for this condition and records a fortunate outcome following its performance.

The case here reported illustrates undue sensitivity to "Pentothal Sodium" with prolonged unconsciousness and respiratory depression, followed by a dramatic response to lumbar puncture. The patient's convalescence was notable, in that post-operative pulmonary collapse developed on the third day.

Clinical Record.

A male patient, aged fifty-nine years, was admitted to the Royal Prince Alfred Hospital, Sydney, for transurethral prostatic resection after an attack of acute retention of urine one month previously. For this, suprapubic cystostomy had been performed at another hospital.

He gave a history of recurrent attacks of bronchitis for the past four years, and on clinical examination of his chest râles and rhonchi were heard at both lung bases. His blood pressure was 180 millimetres of mercury, systolic, and 90 millimetres, diastolic. There was no evidence of cardiac enlargement. Rectal examination revealed a small adenomatous prostate suitable for transurethral resection. A plain X-ray film of his chest showed no active lung disease to be present, but there was some calcification in the left mid-zone which suggested an old tuberculous lesion. Sputum examination did not disclose any tubercle bacilli. The hæmoglobin value was 102% (Sahli), and the white blood cells numbered 7500 per cubic millimetre. Transurethral resection of the prostate was performed, the operation lasting thirty minutes.

"Pentothal Sodium" was given intravenously for anæsthesia, a total of 0·5 gramme of the drug being administered. During the induction the patient became cyanosed. He had an epileptiform fit whilst on the operating table, and at the conclusion of the operative procedure became cyanosed and ceased to breathe. Controlled respiration was carried out by means of the gas machine, the patient's colour remaining good and the pulse of regular rate and normal volume. Picrotoxin was administered intravenously without effect. After six hours' controlled respiration, when the face-piece of the gas machine was removed the patient again became cyanosed and exhibited no respiratory movements. He was therefore placed in the "iron lung", and shortly afterwards had another epileptiform convulsion.

The patient was removed from the Drinker apparatus and lumbar puncture was performed. The cerebro-spinal fluid was clear and its pressure in the vicinity of 300 millimetres of cerebro-spinal fluid. The pressure was reduced to normal. The response shown by the patient was dramatic, normal respiratory rhythm ensuing immediately, and he rapidly became conscious. He caused no further immediate anxiety.

The following day the patient showed slight cyanosis of his lips and ears, but clinical examination of his chest revealed no change from the pre-operative findings, and a plain X-ray film of his chest showed no departure from that taken the day before operation. On the third post-

operative day he began to cough up heavily blood-stained sputum. He did not complain of pain in the chest and he was afebrile. The clinical findings on examination of his chest were diminished movement and dulness on percussion, breath sounds being absent at the base of the left lung. The cardiac apex beat was displaced somewhat toward the left side. Antero-posterior and lateral radiographs of the chest showed partial collapse of the lower lobe of the left lung.

With penicillin therapy his further convalescence was uneventful, he remained afebrile, and the clinical signs at the base of the left lung gradually resolved. Six weeks after discharge from hospital, chest radiography showed that the lower lobe of the left lung was completely aerated.

Summary.

The case reported illustrates the following points:

1. The value of lumbar puncture in prolonged unconsciousness and respiratory depression resulting from undue sensitivity to "Pentothal Sodium".

2. The development of post-operative pulmonary collapse on the third day after operation.

3. The relationship of severe respiratory depression in the presence of bronchitis to post-operative pulmonary collapse.

4. Complete resolution of post-operative pulmonary collapse with conservative measures fortified by penicillin therapy.

Acknowledgements.

I am indebted to Dr. J. W. S. Laidley, of the Department of Urology, Royal Prince Alfred Hospital, Sydney, for permission to publish this case report.

Bibliography.

Bailey, H. (1944), "Emergency Surgery", Bristol, John Wright and Sons, Limited, page 40.

Love, R. J. McNeill (1934), "A Warning Regarding Basal Narcotics", *British Medical Journal*, Volume I, page 327.

POLYCYTHÆMIA TREATED BY RADIOACTIVE PHOSPHORUS.

By B. D. VAUGHAN,
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THE patient, Mrs. R.E.P., aged fifty-seven years, first presented herself on August 8, 1947, complaining of tiredness, irritability, poor memory, morning headaches, "prickly" feeling in the skin and bloodshot eyes; she also suffered from pain behind the sternum when worried or tired. The menopause had taken place seven years previously, and the patient dated her symptoms from about that time. In the meantime she had been under treatment for high blood pressure. There was a family history of similar coloration in two of her brothers.

On examination, the patient was found to be a well-built woman of intelligent and sensible type. Her skin was of a pronounced dusky-red colour, the palpebral conjunctiva was of intense red colour, and the sclerotics and palate were injected. The tonsils were normal, and no glands were palpable in the neck or elsewhere. The heart was diminished in size, the apex beat being one inch inside the mid-clavicular line and the area of cardiac dulness decreased. Her blood pressure was 215 millimetres of mercury, systolic, and 118 millimetres, diastolic; the cardiac rhythm was regular, and no cardiac murmurs were detectable. Examination of the lungs disclosed a small area of bronchial breathing at the apex of the right lung posteriorly, and no adventitiæ. The spleen was enlarged to 1·5 inches below the costal margin. Examination of the urine revealed a faint trace of albumin. A blood count showed that the erythrocytes numbered 7,650,000 per cubic millimetre and that the hæmoglobin value was 128%.

A diagnosis of *polycythæmia rubra vera* was made, and treatment with phenylhydrazine hydrochloride was commenced. This proved to be difficult to control and was abandoned. On January 29, 1948, 4·8 millicuries of radioactive phosphorus (P^{32}) were given intravenously in 300 millilitres of normal saline. A blood count then revealed 7,450,000 erythrocytes per cubic millimetre and a hæmoglobin value of 127%. After the injection there was no immediate alteration in the symptoms; the hæmoglobin value continued to rise, reaching a maximum of 138% on March 4, after which it began to decline; on May 31 the erythrocytes numbered 5,200,000 per cubic millimetre and the hæmoglobin value was 95%. The patient then felt perfectly well and all symptoms had disappeared.

The remission lasted for approximately four months, and then the blood picture returned to approximately the previous level; but the symptoms were considerably milder than previously, and the blood pressure, which had declined, remained at the low level of 145 millimetres of mercury, systolic, and 90 millimetres, diastolic. On April 14, 1949, a second injection of P^{32} was given, this time of 5·0 millicuries. As on the previous occasion, the number of erythrocytes and the hæmoglobin value rose; the latter reached a figure in excess of 140% on May 10, after which it fell; on August 30 the erythrocytes numbered 4,890,000 per cubic millimetre, and the hæmoglobin value was 100%.

In spite of the larger dose, the period of remission was shorter than after the first course of treatment, lasting in all about three months. In November, 1949, all the symptoms had returned, though not to the same degree as in 1947; the spleen was palpable one centimetre below the costal margin, the blood pressure was 190 millimetres of mercury, systolic, and 100 millimetres, diastolic, the erythrocytes numbered 7,800,000 per cubic millimetre and the hæmoglobin value was 147%. A considerably larger injection—6·2 millicuries—of P^{32} was given on November 24. This time there was little apparent alteration in the blood picture; on February 20, 1950, the erythrocytes numbered 7,800,000 per cubic millimetre and the hæmoglobin value was 144%; on March 21 the erythrocytes numbered 7,400,000 per cubic millimetre and the hæmoglobin value was 137%; and on April 17 the erythrocytes numbered 7,200,000 per cubic millimetre and the hæmoglobin value was 135%.

However, the patient's feeling of well-being is much greater than the blood picture would suggest; in fact, it has been noticeable that after each injection clinical improvement took place before the blood picture had greatly improved and lasted after the latter had deteriorated. Of the two generally accepted substances for the treatment of *polycythæmia vera*, phenylhydrazine and radioactive phosphorus, the former proved unreliable in this case and the latter would seem to have lost effect. In view of the fortunate fact that the patient is of blood group O (IV) and Rh-negative, it is now proposed to use her regularly as a blood donor, and thus keep some control on the blood picture pending the development of some more permanent method of treatment.

Reviews.

MALES AND FEMALES.

INTO his book "Males and Females" Roger Pilkington has introduced two ingredients not always present in books of sex education: a healthy sense of humour and an emphasis on genetics.[1] A good idea of the book and of the author's approach may be given by quoting the titles of the chapters and indicating their contents: "One Plus One Equals Three" contains the facts of mating and fertilization; "Like Father, Like Son" explains the development of the individual from the fertilized egg and the role of the chromosomes and genes; "Boy or Girl?" explains the relationship of the chromosomes to determination of sex and also sex-linked characters including lethals; "What Shall We Do with Our

[1] "Males and Females", by Roger Pilkington; 1948. London: Delisle. Sydney: Father and Son Welfare Movement. 8″ × 5½″, pp. 92, with many illustrations. Price: 9s. 6d.

Genes?" discusses some practical applications of genetics in agriculture, stock breeding and the choosing of a human partner; "Sopranos and Basses" deals with the action of the sex hormones with particular attention to the changes of adolescence. A glossary and an amusing index complete the book. The material presented is all sound standard knowledge, elementary, though not too much so, and presented in a thoroughly readable fashion. The illustrations are original and informative. Both moralizing and pornography are conspicuously absent. The book is primarily suitable for young unmarried people of a reasonable grade of intelligence; the author's brand of humour and general approach, as well as a good deal of the information, would probably be lost on the less intelligent. Most older people will enjoy it, if they are not too dull, though it is not directly intended for them. This is a refreshing book, which, placed in the right hands, can do much good.

SOCIAL MEDICINE.

"RECENT ADVANCES IN SOCIAL MEDICINE" by A. C. Stevenson[1] covers an arbitrary selection of topics, in which the author analyses the important changes brought about during the war and in the ensuing post-war years. The subjects discussed are as follows: measurement of growth in children; infant mortality; the health of children in communal day nurseries; the unmarried mother and her child; problem families; school medical inspection; some applications of statistical methods and notes on three subjects of interest, namely, psychosomatic illness and social medicine, the adolescent in industry and "Pulheems". The mysterious "Pulheems" is merely the term used to denote the new system of medical classification as used by the three services and the British Ministry of Labour, the word being derived from the initial letters of the following physical attributes: physical capacity, upper limbs, locomotion, hearing, eyesight (EE), mental capacity and stability (emotional).

All students of the subject and social workers generally will find the book of practical value, and of all the chapters, that upon problem families proves most interesting. Even though such families will be eliminated only in a Utopian civilization, yet all the ways and means to eradicate them, from improved housing to compulsory sterilization, are investigated fully.

AUTOBIOGRAPHY.

"FROM THE HILLS", by John Zahorsky, is the simple yet very interesting autobiography of a pædiatrician.[2] There are three distinct sections, namely, "Development", "Maturity" and "Decline", which interweave to make up the reflections and revelations of a long life of over seventy years, fifty of which were devoted to the practice of pædiatrics. Of Austrian parentage, the author was taken to the United States of America when he was six months old, and the book records his early struggles from farmhouse through backwoods school to town college and later to St. Louis Medical School where he qualified after three years of study.

Surgery did not attract him, and so he decided on child health as his specialty. Although in the book several interesting diagnoses are described, little space is given to purely medical experiences. The author was critical of wholesale tonsillectomy, and also opposed the modern baby nurseries as are found in American obstetrics. As he was for thirty-six years professor of pædiatrics at St. Louis, his wide experience lends much weight to his arguments. The book is light reading and is easily put down and picked up again; at the same time it holds the reader's attention, for many of its chapters indicate the various matters that made up his life's interest—religion (he was deeply religious), poetry, of which he wrote a lot, and also nature studies and psychology. As stated in the introduction: "I have omitted the medical side of my experiences as much as possible. At the end of the book, I have recorded a list of my medical writings, which can be consulted by physicians who may be interested."

[1] "Recent Advances in Social Medicine", by Alan Carruth Stevenson, B.Sc., M.D. (Glasgow), M.R.C.P. (London), D.P.H., with a chapter by Eric A. Cheeseman, B.Sc., Ph.D. (London); 1950. London: J. and A. Churchill, Limited. 8" × 5", pp. 254, with 15 illustrations. Price: 18s.

[2] "From the Hills: An Autobiography of a Pediatrician", by John Zahorsky, M.D.; 1949. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 8¼" × 5¾", pp. 392. Price: 42s.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"An Elementary Course in Philosophy", by George Politzer (translated by Dr. G. P. O'Day, Melbourne); 1950. Sydney: Current Book Distributors. 4¾" × 6¾", pp. 228.

An explanation of materialist philosophy and its relation to dialectical materialism and Marxism, written by "a leading propagandist of the French Communist Party".

"A Manual of Psychiatry", by K. R. Stallworthy, M.B., Ch.B.; 1950. New Zealand: N. M. Peryer, Limited. 5" × 7¾", pp. 308. Price: 25s.

Aims to outline the principles of management of patients with psychological disturbances, and to give a sufficient account of the essentials of psychiatry to meet the needs of the student.

"Light Therapy", by Richard Kovács, M.D.; 1950. Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications, Limited. 8½" × 5½", pp. 120, with illustrations. Price: 16s. 6d.

A lecture on present-day knowledge of the therapeutic uses of "the three divisions of light therapy, including heliotherapy".

"Introduction to Motherhood", by Grantly Dick Read, M.A., M.D. (Camb.); 1950. London: William Heinemann (Medical Books), Limited. 8¾" × 5¾", pp. 104, with many illustrations. Price: 6s.

For the expectant mother.

"Ophthalmic Operations", by Seymour Philps, F.R.C.S.; 1950. London: Baillière, Tindall and Cox. 9¾" × 7½", pp. 408, with 510 illustrations, some of them coloured. Price: 50s.

A new text-book of eye surgery designed for the specialist ophthalmologist and for those pursuing post-graduate ophthalmic studies.

"Worth and Chavasse's Squint: The Binocular Reflexes and the Treatment of Strabismus", by T. Keith Lyle, C.B.E., M.A., M.D., M.Chir. (Cantab.), M.R.C.P. (London), F.R.C.S. (England); Eighth Edition; 1950. London: Baillière, Tindall and Cox. 10" × 7½", pp. 332, with 200 illustrations. Price: 35s.

The previous edition was, in effect, a new book written to take the place of a standard work; it is largely rewritten in this edition.

"Pre-Frontal Leucotomy: A Survey of 300 Cases Personally Followed over 1½-3 Years", by Maurice Partridge, M.A., D.M. (Oxon.), D.P.M. (England); 1950. Oxford: Blackwell Scientific Publications. 8½" × 5½", pp. 504. Price: 42s.

The title is self-explanatory.

"Werdnig-Hoffmann's Infantile Progressive Muscular Atrophy: Clinical Aspects, Pathology, Heredity and Relation to Oppenheim's Amyotonia Congenita and other Morbid Conditions with Laxity of Joints or Muscles in Infants", by Sven Brandt; 1950. Copenhagen: Ejnar Munksgaard. 6¼" × 9½", pp. 360, with illustrations. Price: Danish Kr. 20.

The results of a clinical study.

"The Management of Obstetric Difficulties", by Paul Titus, M.D.; Fourth Edition; 1950. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9½" × 6½", pp. 1062, with 446 illustrations, some of them coloured. Price: £7 7s.

Designed primarily for the specialist in obstetrics, but also for the general practitioner.

"The Surgical Clinics of North America" (issued every two months); 1950. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. Lahey Clinic Number. 9" × 5¾", pp. 348, with many illustrations. Price: £7 5s. *per annum* (cloth binding) and £6 *per annum* (paper binding).

Contains a symposium by 18 contributors on anæsthesia and 22 individual articles ranging widely over the field of surgery.

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All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

SPITTLE.

MAN has ever been enamoured of his excretions and attached to his glandular products. Being his own special creations and representing the secret essence of himself, they were often endowed by him with unique properties. His spittle, therefore, was not a mere glairy fluid that aided digestion, but was incontestably therapeutic and contained as much magic as mucus in its composition. It was rich in promise; and though it often fell short in fulfilment, it was ejected with all the force of faith. It was vital and its properties were various. It was Nature's first nostrum; and soon became the lotion for every lesion, for the savage, like the animal, carried every hurt to his mouth. But it was more than a balm for the wounded flesh; it was a charm of considerable power. The world of the savage was hostile and deceitful. Danger continually threatened the primitive man who never went far without his weapon; but though this may have averted the attacks of man and beast, for the assault of the supernatural he relied to a large extent upon his spittle. He spat to bring himself luck. At the place where danger had been incurred he also spat. Any fancied habitation of the devil received his salivary salute. And when about to cross water in the dark he spat three times.

The spirit world which was formerly ubiquitous has not completely disappeared. Modern man says little about spirits in these days of dynamos and automatic dish-washers; the poltergist has almost perished and table-rapping is practised only by credulous spinsters; but many a person of otherwise sound outlook still crosses his fingers from time to time, touches wood on occasion or throws the spilt salt over his left shoulder to prevent the powers of evil from catching up with him. And so with spitting. To spit on a coin before tossing it is still thought to bring luck. Boys, unwittingly prompted by unconscious forces, often spit to emphasize a pledge. Boxers spit on their hands for luck, as not infrequently the old fish-women spat on their handsel or the first money they received for the day, and having spat upon it, they would kiss it and put it away in a separate pocket, lest it should disappear like a fairy gift. For the act of spitting was thought to bring luck and to exert a powerful charm against fascination and witchcraft. Its virtue was enhanced if the person spat three times, as did the country yokels of days gone by when they saw a piebald horse.

The spittle of kings was like the manna from heaven. It was cherished and jealously guarded; for its power for good and evil was greater than any other spittle. Though in our day the glory of the spittoon has departed and its presence is barely remembered, there was a time when it was almost a sacred receptacle; and the royal spittle of barbaric kings was carefully collected in embossed and precious spittoons by a slave who walked behind the royal presence. The spittle of Mohammed was miraculous; for, not only was the water he washed in sedulously collected, but it is recorded that wherever he spat they immediately licked it up and gathered up every hair that fell from his head. When Hassan, his grandson, was born Mohammed spat in his mouth.

In primitive times the spittle of a human sacrifice was thought to possess a sovereign virtue. In India, women when they beheld a falling star spat thrice to scare the demon. Where the western man, in reconciliation after a quarrel, would shake hands, the East Africans spat upon each other; and when they made a covenant it was sealed by each spitting into the mouth of the other. African natives of another tribe spit upon a stone by the wayside in order to ensure luck for their journey. To spit upon the same stone used to symbolize fraternity was the custom of the colliers of the north of England. Madagascan natives believe that demons cause disease; and when the sick man leaves his infected house he spits towards the door to expedite the departure of his malady. When a pestilence strikes the members of other native tribes they endeavour to drive it away by spitting into a common receptacle and throwing it into the sea. Others spit on the hair of the dead or on the shaven locks of the living before destroying such objects, and thereby safeguard their use by witches. Others again would spit upon a stone and rub their legs with it to allay fatigue. Today the labourer spits into his hands before grasping his shovel.

To the Persian of antiquity spitting was an essentially private business; Herodotus relates that the Persians were forbidden to spit or to make water in the presence of another. Spittle was important to the Israelite, for if he suffered from any discharge and his spittle touched another person that person was regarded as unclean. If the Hebrew widow of the eldest son could not persuade a younger son to marry her, she could summon him before the elders and, loosening the shoe from his foot, she could spit in his face and imprecate a curse upon him. This was a sign of contempt which has persisted through countless generations. The Christian Saviour suffered a similar contempt when the Roman soldiers spat upon Him and mocked Him before the crucifixion. Nor was He the only one who has suffered the world's disdain from the loaded lips of the populace. Man spits out his disgust at any vile thing. Such expectoration, as it were, removes

the nasty taste which may have metaphorically menaced his mouth. At one time the infant at its baptism had salt thrust into its mouth so that it could spit out the devil. Men used to spit when they heard the devil's name, as they often do at a revolting spectacle or at a person whose conduct fills them with loathing. Thus Antonio spat upon the Jewish gaberdine of Shylock and called him a dog. When Gloucester wooed the bereaved Anne whose husband he had lately killed, she spat at him and said: "Would it were mortal poison, for thy sake." And Robert Browning, hearing some derogatory remark about his late wife from Edward Fitzgerald, wrote to "The Athenæum" offering to spit in Fitzgerald's face, but refrained, for:

> Surely to spit there glorifies your face—
> Spitting—from lips once sanctified by Hers.

"Sacred spittle bring ye hither", sang Herrick in constructing his charm against the evils of witches and warlocks. For the superstition of the spittle was great and its powers against evil were manifold. When the fear of fascination was rife wise men took the advice of Theocritus and spat three times in their bosoms. Those who had become unpleasantly arrogant were bidden to do likewise. It was thought better to do this than to suffer the malefactions of the unseen. A similar ritual was solemnly performed at the sight of a madman or an epileptic. Even the nursemaid used her spittle to save the sleeping infant from the bewitchment of an evil eye, sometimes by spitting in the four corners of the room, sometimes by moistening her finger with saliva and rubbing the child's eyelids or by licking the bratling's brow. In the Roman baptismal rites the priest exorcised with spittle the ears and nostrils of the infant. In this connexion, in his translation of the second satire of Persius, Dryden says:

> Th' obscure old grandam, or the next of kin,
> The new-born infant from the cradle takes,
> And first of spittle a lustration makes:
> Then in the spawl her middle finger dips,
> Anoints the temples, forehead, and the lips.

Spittle was thus highly prophylactic; but its curative qualities were equally great and found varied use in the gloomy pantomime of witchcraft. To unbewitch the bewitched, according to Reginald Scot, it was necessary to spit into the pot where you had made water, or to fill your shoe with saliva before putting it on.

Though from Biblical times it was counted as a cure for leprosy, spittle was chiefly applied in the ancient practice of ophthalmology. When Thoth, the medicine god of Egypt, spat upon the injured eye of Horus his wound healed and he recovered his sight. When Christ cured blindness, he adopted the simple expedient of spitting on the ground and making clay of the spittle and of anointing the blind man's eyes with the clay. Impediments of speech and deafness were in a like manner cured by the Saviour, who put His fingers into the deaf ears and spat, and then touched the tongue and the deaf mute's silent world became audible. Midwives used spittle extensively as a collyrium. Lithuanian mothers often licked their babies' eyes when smitten with conjunctivitis. Palestinians used to remove foreign bodies from the eye by licking the naked eyeball with their tongues. Thinking her spittle possessed specific qualities, a German woman is reported to have licked the eyes of thirty-four syphilitics in order to combat the infection. The spittle of the firstborn was valuable, but that of the seventh son of the seventh son was of inestimable value as a therapeutic agent. Fasting spittle had a dermatological use. When a man had neither eaten nor drunk his spittle was thought to cure "all tetters, itch, scrabs, pushes, and creeping sores", the bites of spiders, ants and other crawling things. Sir Thomas Browne believed that fasting spittle might cure snake-bite. To cure the King's Evil or any soreness of the throat it was necessary for a fasting virgin to lay her hand upon the place and then spit three times upon it. A woman in labour might call upon the priest, who, having repeated an incantation, would spit in her face and leave the rest to Nature or to the common sense of the midwife. Knots once possessed the double power of causing or curing disease. Their magic was greater if they were spat upon. Lastly, saliva was once thought to embody the fertility principle and was often given to barren women as part of a magic potion. A favourite recipe used by the women in West Prussia was the saliva of stallions, believed specially potent for those who had not been graced with an issue.

David once feigned insanity by scrabbling upon the doors of the gate and letting his spittle fall down upon his beard; and apparently he was successful in his design and escaped capture, for his methods were those of the dement and the idiot who may allow their saliva to run unchecked upon their chins. The ways of madmen are many and strange, but the circumstance of their spittle does not establish a diagnosis. The schizophrenic, for instance, may slobber indifferently or spit upon the ground with a maddening perseverance. The paretic's tremulous lips may become frequently slavered. The mental defective may drool. Ptyalorrhœa may assail the neurotic; while a salivary excess may characterize quinsy and frothing at the mouth occur in the epileptic. The patient with bulbar palsy may suffer a superabundance of spittle improperly directed, and that from the buccal catchment of the Parkinsonian may trickle down the spillway of the lower lip. These and other diseases of the central nervous system or such as cause a general stomatitis belong strictly to the province of the physician. For apart from such disorders the modern man's spittle gives scarcely any concern. Though his hungry mouth may water at the sight of good things, he regards it without awe, and its presence is accepted without qualification. Only the hypochondriac is likely to pay undue attention to his spittle, wondering if his anguished lips are too dry or whether, like his pride, he should swallow his salivary secretions. The ordinary man suits his inclination and spits without recollection or clears his throat without concern. If he spits in disgust, he goes through no salivary ritual. The new moon leaves him unmoved. No ghost is laid by his gob; nor are the forces of evil turned aside by his rheum. He finds no use for his fasting spittle. Though he may say his prayers, he seldom spits upon his sins; and having a bad dream occasions no desire to spit over his left shoulder. Manners have taken the place of magic, and spitting has declined with sorcery. Courtesy prevents spitting in public; cleanliness controls it in the home. And common sense counsels a man from spitting at the heavens—lest it fall back in his face.

Current Comment.

CURIOSITIES FROM MEDICAL CUPBOARDS.

Strange things come out of cupboards, especially hospital cupboards, and W. P. U. Jackson[1] has been rummaging with a zeal that would delight any ward sister. His cupboards are in the odd corners of medical and, especially, nursing practice, and he has produced not skeletons but private pets, very much alive though pale and blinking in the light of day. He takes as his text the words attributed to Charles II: "My Lords, I fear I am an unconscionable time a-dying." The appropriate moral for the favourite irrationalities of doctor or nurse needs no pointing. Those who think that what he drags, shrinking or brazen, from the cupboard are corpses or shadows, should look around again, especially in hospital, and then bend themselves to the dispatch. First, here is a hospital employing some 300 trained nurses wasting at least 200 nurse-hours a week so that cut flowers may be taken from the wards at night and rearranged in the morning; all because Ingen-Harz found in 1779 that flowers respire like animals at night, using up oxygen and emitting carbon dioxide. It is apparently not noted that even if cut flowers respired "as vehemently as growing plants, it would take some thousand hydrangeas to have the effect of one patient", and some little reliance might still be placed on the ventilation and air space provisions of modern hospitals. Next on the list is the practice of nursing between blankets patients with acute rheumatism and acute nephritis. It is hard to find grounds justifying this for therapy or for convenience, yet Jackson quotes a reference advocating it as recently as 1949. Conversation about, and within hearing distance of, an apparently unconscious patient, who is being anæsthetized or is comatose from an illness, should have succumbed not so much to advancing science as to common sense, yet Jackson can quote his own experience of two nurses making his bed when he had septicæmia. Said one, "He looks pretty bad, doesn't he?" And the other, "Yes, the doctors don't expect him to get better". It would be reassuring to know that this practice was dead during ward rounds in teaching hospitals. We know that it is not. We may hope that the next practice mentioned, fumigation of sick-rooms with sulphur, formaldehyde and the like, has been discarded; but we cannot be so sure that a room or bed recently occupied by a patient who has died, from whatever cause, will not undergo a ritual cleansing quite disproportionate to that for a patient recovered from, for example, a throat or wound infection. Sterilization methods for instruments and skin are, of course, still matters of argument, but quaint, indefensible practices survive. Perhaps it is becoming generally realized, as Jackson states, that sterile water does not long remain sterile once its container has been opened, that the laying of instruments in shallow dishes of spirit is bad practice, and that the dipping of an instrument in boiling water or in some disinfectant does not sterilize it, but the practice of smearing ether, spirit, flavine and similar substances on a skin surface or a rubber bottle cap gives no warrant to regard the surface as sterilized. Jackson quotes evidence that iodine in spirit is the only common rapid surface disinfectant and describes as correct the London Hospital method of application: the tincture is painted on the skin, and then after half a minute the iodine stain is removed with either ether or spirit on another sterile swab. The constipation question has been widely discussed, and the rational position is well known. Perhaps the prescribing of purgatives is now minimal, but it would be interesting to know how many ward sisters still require a daily tick on the bowel chart, how many purgative pills are handed out in wards, and how many unnecessary enemata are given, with their possibility of producing colo-proctitis or generalized rash. Jackson states that it is said that enema rash is known only in English-speaking countries, because the use of soap as enema material originated when, many years ago, the English translator of a French treatise jumped to the conclusion that the word *lavage* implied soap as well as water. The alleged unsuitability of mother's milk for the baby and other spurious reasons for the cessation of breast-feeding are probably less common in Australia than in some other countries, so that we need not linger on the point. Fear of administration in adequate amounts of morphine—and of other analgesics and sedatives—is, however, a serious matter. As Jackson points out, severe pain in acute disease requires relief, and in chronic killing disease addiction seems hardly of much concern. It is essential, of course, that dangerous drugs be used with care and that their contraindications be understood, but a hypercautious attitude is wrong if the patient suffers. Many nurses, incidentally, have quite unjustified ideas on the capacity of barbiturates and the like to produce addiction. "Tonics" have been sufficiently "debunked", but even here the practitioner must muster his reason and common sense against the patient's insistence. Of Jackson's last point, the survival of scarlet fever as a separate entity with appropriate respect to its infectious nature not generally accorded to other streptococcal throat infections, we need say little; it is not perhaps of the same type as the other points he raises. But his paper is commendable. There is nothing new in it, as he is the first to admit, but if anyone doubts that the practices mentioned (and others) still survive, with their echoes of antiquity, we can only borrow the exhortation that is peculiarly Sir Christopher Wren's own and say: "*Circumspice.*"

[1] *The Lancet*, August 26, 1950.

THE FEDERAL MEDICAL WAR RELIEF FUND.

Two relief funds, administered by trustees appointed by the Federal Council of the British Medical Association in Australia, exist to provide financial assistance to the dependants of deceased medical officers of the two world wars. Most members of the medical profession know of these funds, many have contributed generously to them, but it is important that the funds should not be overlooked, especially the more recent of the two. For this reason we draw attention to certain facts brought out by the respective trustees in their reports for the year ended June 30, 1950.

The Medical Officers' Relief Fund (Federal), which was established in 1918 to provide financial aid to the dependants of deceased medical officers of World War I, is in a satisfactory position. Help is still being granted to seven beneficiaries, the total amount paid during the year being £562. Of this one claim met in New South Wales absorbed £100, one in Queensland absorbed £104, four in Victoria absorbed £306 and one in South Australia absorbed £52. The total revenue from investments was £298.

The Federal Medical War Relief Fund, which is concerned with the dependants of deceased medical officers of World War II and is still open for receipt of donations, is the one requiring special attention. During the year three claims met in New South Wales absorbed £171, ten in Queensland absorbed £1080, two in Victoria absorbed £156 and two in South Australia absorbed £104; these sums with £27 for management expenses made up a total outlay of £1538. However, the income received from investment of funds amounted to only £628, leaving a deficiency of £910 to be met from the funds themselves. The trustees are anxious that the fund should be built up sufficiently to make its income-earning capacity nearer to the amount of financial assistance they are called upon to provide; in this way the funds could be preserved intact to provide for possible claims over many years to come. Additional contributions received through the various Branches of the British Medical Association during the year amounted to £301 from New South Wales, £22 from Queensland, £10 from Victoria, £5 5s. from Western Australia and £5 from South Australia, making a total of approximately £343. These gifts are appreciated, but further liberal giving is necessary if the aim of the trustees is to be achieved, and if continued practical expression is to be assured of the profession's loyalty to former colleagues.

Abstracts from Medical Literature.

RADIOLOGY.

Unresolved Pneumonia.

C. L. HINKEL (*American Journal of Roentgenology*, March, 1949) deplores the indiscriminate and inaccurate use of the term "unresolved pneumonia" and supports a methodical course of procedure for exclusion studies. He considers that study and care of pneumonia patients should be continued until all pulmonary shadows have disappeared or are proved to be due to fibrosis. True unresolved pneumonia is rare, while bronchiectasis, atelectasis and intrabronchial diseases are more common.

Pulmonary Embolism Without Infarction.

R. SHAPIRO AND L. G. RIGLER (*American Journal of Roentgenology*, October, 1948) state that in pulmonary embolism without infarction the characteristic finding is ischæmia of the involved pulmonary segment. This is represented by a segmental area of increased radiability on the chest X-ray film. Central to the site of the embolism the vascular pattern is well outlined, while in the area itself the vascular pattern stops rather abruptly. In addition, there are often increased density and sharper demarcation of the involved vessel. The local area with diminished or absent vascularization corresponds to the pulmonary segment supplied by the embolic artery. These findings are in striking contradistinction to the usual area of increased density on the film in cases of pulmonary embolus with infarction. The area of increased radiability due to pulmonary embolism without infarction must be differentiated from partial bronchostenosis with obstructive emphysema and also from localized areas of non-obstructive emphysema. In obstructive emphysema, the changes during expiration, with the shift of the mediastinum toward the normal side and the depression of the involved diaphragm, serve to differentiate these two conditions. Localized areas of non-obstructive emphysema may be somewhat more difficult to distinguish. However, the abrupt termination of the vascular pattern at the site of the embolus is usually sufficient to make the diagnosis.

Cavitary Form of Pulmonary Neoplasm.

F. ISAAC AND R. E. OTTOMAN (*Radiology*, May, 1949) state that early differential diagnosis between inflammatory and malignant lesions of the lung is not always possible. Moreover, no pathognomonic signs of pulmonary neoplasm exist at any stage of the disease, either clinically or radiographically. Cough, hæmoptysis, pain in the chest and weight loss in a patient over forty years of age must be assumed to indicate a pulmonary neoplasm until proved otherwise. The type of pulmonary neoplasm most often confused with infection is the cavitary form of bronchogenic carcinoma. Radiologically, the lesion often presents a rather well-circumscribed, round or ovoid appearance, suggesting an infected fluid cyst or, when small, a tuberculoma. At other times the infiltration is more diffuse, simulating pulmonary abscess or ulcerating tuberculosis. The cavity is often eccentric, and the contours of the inner wall have an irregular, ragged or "bumpy" appearance, corresponding to the irregular tissue necrosis within the tumour. This is especially well brought out by body section radiography. In the conventional chest film a large portion of the inner wall may be obscured by the fluid within the cavity. In the planigram, however, the fluid gravitates into the posterior recess of the cavity, and anterior to this, the whole circumference of the cavity wall is well demonstrated. The authors emphasize this irregular "bumpy" character of the cavity wall in neoplastic disease. It has been described often before. It is not claimed to be a pathognomonic sign of cancer; it may be found at times in other conditions, especially in tuberculosis. It should be stressed, however, that its occurrence is frequent in malignant disease, and, when recognized, it will direct early attention to the true nature of the lesion.

A Type of Pneumonokoniosis.

ARTHUR A. HOBBS, JUNIOR (*American Journal of Roentgenology*, April, 1950), states that the principal clinical indications of talc pneumonokoniosis, dyspnœa, cough, cyanosis, clubbed fingers and diminished vital capacity, are common to all types of disabling pneumonokoniosis. The specific relation to asbestosis is remarkable when the clinical picture is correlated with X-ray findings. The early radiographic manifestation in either disease is lung field haziness, fine reticulation or soft nodulation, which may be so delicate as to escape detection. It is quite unlike the distinct nodulation typical of silicosis. As disease progresses, the parenchymal pulmonary lesions gradually become denser and tend to become confluent, developing asymmetrically with compensatory emphysema, without nodulation and with a predilection for pleural involvement. Such X-ray changes observed in talc pneumonokoniosis have also been described for asbestosis. As clinical indications of unfavourable prognosis, anorexia and weight loss have been noted in both diseases.

Short Œsophagus.

D. WALDRON SMITHERS (*British Journal of Radiology*, May, 1950) reviews the evidence in support of the theory that both congenital shortening of the œsophagus and acquired shortening due to cicatrization following ulceration are comparatively rare, and that the majority of cases diagnosed as short œsophagus radiologically are primarily cases of hiatus insufficiency associated with spasm of the longitudinal muscle fibres of the œsophagus. Herniation of the cardia into the mediastinum interferes with the valve control and allows acid to flow into the œsophagus. Œsophagitis and peptic ulceration may follow the regurgitation. Shortening of the œsophagus, due to contraction, may result from reflex stimulation due to irritation from some abnormality in the œsophagus or upper part of the abdomen, and either may pull part of the stomach through a lax hiatus, or may follow herniation, due to some other cause, when irritation due to regurgitation of gastric contents causes the contraction which then takes up the slack. In some cases the shortening may become permanent owing to fibrosis and fixation, but the comparative rarity of post-mortem reports of such cases and the way in which the herniation can often be reduced at operation suggest that this does not usually occur. The development of cancer has been noted in a few of these cases; four new instances are reported here. Three possible reasons for the association are discussed: firstly that it may be a chance occurrence, secondly that the œsophagitis that results may predispose to the development of cancer, and thirdly that the carcinoma acts as an irritative focus causing contraction of the œsophagus and at the same time increases intraabdominal pressure, so helping to dilate the œsophageal hiatus and predisposing to herniation.

Chordomata.

E. H. WOOD, JUNIOR, AND G. M. HIMADI (*Radiology*, May, 1950) present an X-ray study of 16 proved cases of chordoma. They state that chordomata of the clivus cause destruction of the sphenoid bone in the great majority of cases. The tumour commonly extends into the sphenoid sinuses, often into the naso-pharynx, and occasionally into the ethmoid region. In the intracranial tumours, calcific particles are frequently demonstrable radiologically. Encephalography and ventriculography are valuable procedures for establishing the diagnosis of chordoma. The third ventricle usually is displaced upward, while the cerebral aqueduct and fourth ventricle are displaced backward. The tumour is outlined discretely by gas in the subarachnoid cisterns. Vertebral chordomata characteristically produce osteolysis of two or more vertebræ and invade the intervertebral disks. Extraosseous extension of the tumour occurs in any direction. Osteoblastic reaction may be encountered in the vertebral column associated with bone destruction. Whenever a mixed osteoclastic and osteoblastic reaction is observed, the diagnosis of chordoma must be considered.

Fibrous Dysplasia of Bone.

LIEUTENANT A. W. MANN, M.C., O. EITZEN, M.D., AND E. P. MCNAMEE, M.D., present a case of fibrous dysplasia of bone showing polyostotic involvement and unilateral thickening of the skull. They state that the ætiology of this disease is obscure. The prevailing opinion is that it is due to a developmental defect. It is characteristically discovered in childhood or early adolescence. A pathological fracture may be the first indication of the disease or a limp with pain or deformity of the lower limbs may be the chief complaint. Facial asymmetry, ocular proptosis, and acromegalic changes may occur at times. The extraskeletal abnormalities are pigmentation of the skin, sexual precocity and endocrine dysfunction in female patients mainly, and hyperthyreoidism. Laboratory findings are frequently negative in this disease. The blood phosphatase level, however, may be elevated. Although the histopathological picture is not entirely charac-

teristic, a biopsy is of aid and should be performed, if possible, in all cases when this disease is suspected. It seems evident that although fibrous dysplasia has been looked upon as a cystic bone disease, cysts if present are an insignificant and secondary part of the lesion. The rarefied areas in the bone are ordinarily solid lesions, composed of collagenous connective tissue in which there may be small foci of ossification. In the main, the areas of bone show little osteoblastic activity. They are thought to represent metaplasia from the connective tissue. The calcification may be irregular, but in this case was fairly uniform. Occasionally, metaplastic foci of cartilage have also been found. Cysts, when present, are apparently the result of degeneration, necrosis or hæmorrhage. Only insignificant numbers of lymphocytes are present; consequently the lesions are evidently not due to inflammation. No evidence of neoplasm has been found in any of the cases. Fibrous dysplasia of bone has been found to be a self-limited disease. The activity of the disease process decreases with advancing age and is quiescent in adults. There is no therapy indicated in this disease except occasional bone curettage or rib resection of monostotic lesions. It may rarely be advisable to perform massive autogenous bone grafts to strengthen long bones which have undergone pathological fractures or are in danger of doing so. Generally, however, conservative treatment of these cases with proper caution against trauma and severe exercise in an effort to avoid spontaneous fractures is advisable.

PHYSICAL THERAPY.

Wilms's Tumour: Evaluation of Treatment Methods.

ROLFE HARVEY (*Radiology*, May, 1950) reviews the literature in an attempt to analyse the value of pre-operative and post-operative irradiation in the treatment of Wilms's tumour. He states that five methods of treatment are available. The first, irradiation alone, is advocated by Dean, of the Memorial Hospital, who has reported a series of 20 cases of Wilms's tumour, in five of which the patient survived for over five years. It is still commonly stated that no cure has resulted from irradiation alone, but in many cases, some inoperable, proved by biopsy, the patients have been reported alive and well ten years after treatment. The reports of irradiation in early or operable cases are few, and most are unproved histologically. The second method is surgery alone. A strong advocate of this is Ladd, of Boston, who considers that pre-operative irradiation is dangerous. Ladd's figures show 13 survivals from 54 nephrectomies without irradiation. In support of the third method, pre-operative irradiation *plus* surgery, are the facts that large inoperable tumours may lessen in size sufficiently to allow of removal, and that greater ease of operability reduces shock and lessens the danger of metastases at operation. The fourth method is surgery *plus* post-operative irradiation. Cases have been reported in which retroperitoneal extension, discovered at operation and treated by post-operative irradiation, has been followed by survival over four to eleven years. Figures from the Boston Children's Hospital show that the survival rate has been raised from 32·2% to 47·3% by an improvement in the technique of irradiation and an increase in the dose given. The surgical procedure remained the same. These figures appear to the author to be significant. The fifth method, pre-operative irradiation, surgery and post-operative irradiation, seems to be the method most commonly employed at the present time. The survival rate from clinics using this method surpasses all others. It seems therefore that neither surgery nor irradiation alone is adequate in the control of Wilms's tumour. The method of yielding the best results at the present time is surgery combined with pre-operative and post-operative irradiation.

X-Ray Therapy of Primary Inoperable Carcinoma of the Breast.

RUTH GUTTMAN (*Radiology*, April, 1950) reports 82 cases of inoperable carcinoma of the breast, proved by biopsy, in which the patients were completely followed up and received no treatment except X-ray therapy. She states that a wide area was irradiated, many fields being used; the technique is fully described. The aim was to give a tumour dose of 3000*r* to 4000*r*; this generally occupied about six weeks. Untoward reactions were not great. About 4% of patients complained of shortness of breath and dyspnœa, but these symptoms usually decreased after twelve months or so. A statistical analysis is not given, but the author states that 20 patients have survived over five years, and 14 of these were apparently free of disease at the end of that time. One striking case was that of a woman, aged twenty-seven years, with a carcinoma of the breast, occurring during pregnancy. When she was first examined, both breasts were involved and metastases were evident in bone. The breasts and various bone lesions were treated, and the patient was sterilized. She has been well and apparently free of disease for over eight years. The author stresses the fact that few patients with this condition are beyond help, and that it is difficult to judge beforehand which patient is likely to respond to treatment and which will not. In many of the apparently hopeless cases the patients have shown remarkable improvement, and few should be regarded as beyond aid.

X-Ray Therapy of an Advanced Cervico-Uterine Cancer.

F. BACLESSE (*American Journal of Roentgenology*, February, 1950) states that in order to obtain accurate information concerning effective dosage and technique, 78 patients with advanced uterine cancer were treated by X-ray therapy alone from 1930 to 1942; all lesions were Stage III and Stage IV. Of the 78 patients, 14 are alive and apparently well five years after treatment. The authors draw the following conclusions. Of the seven patients with pronounced vaginal involvement, four have remained well, and it seems that with spread along the vagina the outlook is more hopeful as regards cure than with parametrial involvement. In all the five-year survivals the patients were treated at 200 kilovolts. In the early cases large fields were used, but these have now been discarded. Fields of 150 or 120 square centimetres are now used. In this way, skin and bladder reactions are reduced to a minimum. Also the treatment time has been extended from five weeks to ten weeks. A total skin dose of 20,000*r* to 25,000*r* is given, distributed over six or seven fields, giving in most cases a tumour dose between 4300*r* and 7100*r*. Two anterior pelvic fields are used, with three posterior fields and two small perineal fields directed to the obturator foramen. Occasionally a direct intravaginal field is added. It is possible by this means to give an adequate tumour dose without excessive skin damage. The author states that moist skin reactions as well as bladder and intestinal reactions should be avoided, and can be avoided by fractionation.

Radiation Therapy of Acute Pancreatitis.

LEO LEVI AND ROBERT ENGLE (*Radiology*, April, 1950) report a series of 28 cases of acute pancreatitis treated by X-ray therapy from 1941 to 1948. The technique of treatment varied, but generally the factors were 140 kilovolts with a filter of 0·25 millimetre of copper. A dose of 75*r* was given, usually only once, but occasionally repeated. Two of the patients died. Analysis of the results suggests the following observations: (i) No response to treatment can be noted in terms of fever or diastolic activity of the blood. (ii) Recurrences were not averted or sequelæ prevented. (iii) Definite clinical improvement followed X-ray therapy in relief of nausea, pain and distension. (iv) The low mortality figures indicate that X-ray therapy is of great value. The authors state that acute pancreatitis has a mortality rate of 21·3% when treated by conservative measures and 44·7% when treated surgically.

NEUROLOGY AND PSYCHIATRY.

Constipation in Disseminated Sclerosis.

LEO HESS (*The Journal of Nervous and Mental Disease*, February, 1950) describes characteristic visceral disturbances in multiple sclerosis. In addition to the well-known entities such as disturbances of the bladder and genital disorders including impotence, he draws attention to constipation. This occurred in nine of the 22 cases. The ingesta are chiefly retained in the proximal portion of the colon. This appeared to be dilated and almost free of haustration. However, the distal portions of the transverse and the descending colon were deeply segmented, and the shadow in contrast to the large, unhaustrated ascending colon appeared to be narrow; the content, which in the ascending colon is homogenous, in the descending colon was broken up into larger or smaller particles. The contracture of the aboral part of the transverse and of the descending colon resembled the contracture and cartilage-like firmness of loops of the small intestines around the umbilicus, such as may be seen in tabetics at the time of the crises gastriques.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on June 22, 1950, at the Royal North Shore Hospital of Sydney, Crow's Nest, New South Wales. The meeting took the form of a number of clinical demonstrations by members of the honorary medical and surgical staff of the hospital.

Pyelonephritis.

DR. F. A. E. LAWES showed a male patient, aged fifty-nine years, who had been admitted to hospital on April 25, 1950, suffering from nausea and anorexia of six months' duration. Vomiting had been present for two weeks and vague abdominal pain for one to two weeks, with a rise in temperature to 100° F. The previous illnesses included jaundice three years earlier, for which he had had three months' treatment, and drainage of a scrotal swelling one week prior to his admission to hospital. On his admission to hospital the patient was mentally retarded and vague about his history. His abdomen was distended, and tenderness was present in the left lumbar region and the left renal angle. No abnormality was detected on rectal examination. On May 1 ascites was noted, and a tender, vague mass was palpated on the left side of the abdomen. The patient's general condition deteriorated as the blood urea level rose, until May 20, when it began to improve. He had intermittent pyrexia, his temperature rising to 104° F. on one occasion. A number of special investigations were carried out. On April 26 the hæmoglobin value was 10·5 grammes *per centum*, the leucocytes numbered 12,000 per cubic millimetre and the blood sedimentation rate was 21 millimetres in one hour. On May 29 the hæmoglobin value was 8·2 grammes *per centum*, the leucocytes numbered 12,300 per cubic millimetre and the blood sedimentation rate was 22 millimetres in one hour. The blood urea content was estimated on four occasions between April 29 and June 8, with the following results: 120, 290, 61 and 68 milligrammes *per centum*. Repeated tests for occult blood in the fæces gave negative results. The Wassermann test failed to produce a reaction. On May 3 the serum protein content was 6·6 grammes *per centum*, the albumin-globulin ratio was 1·75:1·0, the serum bilirubin content was 0·3 milligramme *per centum* and the thymol turbidity was 2·5 units. Cultural examination of the urine produced growths of the following organisms: April 27, *Bacterium coli*; May 6, *Streptococcus fæcalis*; June 1 and 7, *Pseudomonas pyocyanea*. At a cystoscopic examination on May 5, the bladder floor was seen to be covered by massive bulbous œdema, the ureteric orifices and interureteric bar being completely obscured. At a sigmoidoscopic examination on June 15 the instrument was passed for a distance of 13 centimetres; no carcinoma was seen; there was some thickening of the anterior rectal wall. Excretion pyelography was carried out on May 1. The outline of the left kidney was not identified, and there was no apparent function on that side. The outline of the kidney appeared in the fifteen minute film; it was symmetrically enlarged. Function was present on that side, and the right ureter was dilated in its upper half. X-ray examination after a barium enema revealed no lesion in the colon.

Dr. Lawes said that the patient was gravely ill on his admission to hospital with all the signs and symptoms of uræmia. The obstruction to his left kidney was at first thought to be due to a carcinoma of the colon. Investigation showed that that was not so, and it was interesting to try to discover where the obstruction began. The patient's condition improved spontaneously when he began to pass more urine, and at the time of leaving hospital he was much better; but he still had some anæmia and a low-grade fever. He refused operation, so the nature of the lesion was not determined.

General Paralysis of the Insane.

DR. F. H. HALES WILSON, DR. R. A. R. GREEN and DR. A. H. B. CHANCELLOR presented a female patient, aged forty-nine years, suffering from general paralysis of the insane. She had been admitted to hospital on May 17, having suffered from attacks of loss of consciousness for four years. Her first husband had been killed in the first World War; she had remarried in 1942. She had had no children, no miscarriages, and no previous illnesses. She was unable to describe the attacks of unconsciousness. Her husband said that she was growing slower in her movements, and that she had been forgetful and had lost some of her previous interests—for example, card games. She had also recently become more suspicious and suffered from imagined slights. The patient herself did not give that history, merely stating that she consulted the doctor because of pain in the abdomen. On examination of the patient, no abnormality was detected in the cardio-vascular system, the respiratory system or the alimentary system. Examination of the central nervous system gave the following results. The pupils were eccentric; the left reacted sluggishly to light and the right normally, and both reacted to accommodation. No abnormality was detected in the fundi, and the cranial nerves were intact. Touch and pain sensation were present. The biceps, triceps, supinator, knee and ankle reflexes were present, and the plantar reflexes were flexor; all abdominal reflexes were absent. Coordination was good. The patient's cerebration was very slow, and her concentration was poor. Her memory appeared poor, and some confusion was apparent. A number of investigations were carried out. The blood reacted to the Wassermann test. Examination of the cerebro-spinal fluid obtained by lumbar puncture gave the following results: the fluid contained 10 lymphocytes per cubic millimetre, the protein content was 50 milligrammes *per centum*, the chloride content was 720 milligrammes *per centum*, the sugar content was 67 milligrammes *per centum*, the Wassermann test produced a positive reaction, and the Lange cold curve was represented by the figures "5555543100". A blood count gave the following information: the erythrocytes numbered 3,910,000 per cubic millimetre, the hæmoglobin value was 11·7 grammes *per centum*, and the leucocytes numbered 6300 per cubic millimetre, 67% being neutrophile cells, 3% eosinophile cells, 28% lymphocytes and 2% monocytes. Penicillin therapy was commenced on May 19, a dose of 200,000 units being given every four hours. On May 24 the cerebro-spinal fluid findings were complete, and it was decided to institute malarial therapy. On May 29 four millilitres of malarial blood (benign tertian) were injected intravenously. Fever began on June 3, and after eight rigors quinine therapy was instituted, starting with five grains three times a day on June 18. On June 19 the patient had a further slight rigor, her temperature rising to 101·6° F.

The comment was made that at the time of the meeting the patient's mental condition was very little different from its original state. A blood count gave the following findings: the erythrocytes numbered 2,310,000 per cubic millimetre, the hæmoglobin value was 7·4 grammes *per centum*, and the leucocytes numbered 6400 per cubic millimetre, 90% being neutrophile cells, 1% basophile cells, 8% lymphocytes and 1% monocytes.

Pneumomyelography in the Diagnosis of Intervertebral Disk Lesions.

DR. DOUGLAS ANDERSON exhibited X-ray films illustrating the use of pneumomyelography for demonstrating protrusion of an intervertebral disk into the vertebral canal (or the absence of such a lesion). The X-ray examination of the lower lumbar and sacral region of the vertebral canal had been carried out after the introduction of some 10 millilitres of air into the spinal theca by means of lumbar puncture. During the procedure the patient lay on a table tilted just sufficiently for the air to rise to the lowest limit of the subarachnoid space. Dr. Anderson stated that the method had the advantages over myelography by means of the introduction of iodized oil into the theca that the outline of the structures on the posterior wall of the vertebral canal were beautifully displayed, that the contrast medium was soon absorbed so that arachnoiditis was not to be feared, and that a needle of fine gauge could be used for the lumbar puncture. The patient should be advised not to sit up during the rest of the day after the lumbar puncture, for if the air in the theca should rise into the cranium a rather bad headache would result, as after pneumoencephalography. Although the method had been described in 1933 and had the advantages mentioned over myelography with iodized oil, it did not seem to have yet come into very general use.

Peripheral Vascular Disease (Arteriosclerosis).

DR. JAMES ISBISTER showed a male patient, aged sixty-two years, suffering from peripheral vascular disease in the right lower extremity. Pain on exertion in the right buttock and the right calf had been present for three years. He also suffered from cramp in the right leg at night, and the right foot became cold and pale. On examination of the patient in January, 1950, no pulsation was detected in the right femoral artery or in any of the arteries below

that level on the right side. On elevation of the right leg there was excessive blanching, which was followed by excessive redness on dependency. The blood supply to the left lower extremity was normal. It was decided that the patient had partial obstruction in the right external iliac artery, which had occurred fairly suddenly three years previously. He was admitted to hospital, the intention being to treat him with intermittent venous occlusion, though it was feared that good results could not be expected on account of the high level of the obstruction. He was treated with bed rest and intermittent venous occlusion for sixteen hours a day for three weeks, and then discharged from hospital. Since then he had been having intermittent venous occlusion for two or three hours each day. He could walk up to half a mile at an ordinary pace with slight discomfort.

Dr. Isbister demonstrated three forms of apparatus which automatically performed intermittent venous occlusion: (i) a hydrostatic method, which was said to be simple and cheap to make, and could be operated from a water tap (originally described by C. Wilson and A. G. Ogston in *The Lancet*, Volume I, 1938, at page 606); (ii) an electrically driven machine made by Clements, of Saint Leonards, New South Wales; (iii) an electrically driven machine designed by Shillingford, of London. Dr. Isbister said that the third machine was the one which the patient had used both in hospital and at home; it had the advantage of being readily portable and silent in operation.

Dr. Isbister said that intermittent venous occlusion had fallen into disrepute in some quarters, like many other methods for the treatment of peripheral vascular disease. The essential part of the treatment appeared to be its continuance after the patient had returned home. The method of intermittent venous occlusion was eminently suitable for use in the patient's home.

Hereditary Hæmorrhagic Telangiectasia.

Dr. Isbister next showed a female patient, aged sixty-four years, suffering from hereditary hæmorrhagic telangiectasia. The patient had been admitted to hospital on May 9, 1950, because of severe epistaxis, which had reduced her hæmoglobin value to 3·6 grammes per 100 millilitres. The hæmorrhage was controlled by nasal packing, and her blood loss was made good by blood transfusion. She gave a history of repeated severe epistaxis for twenty-seven years; on three previous occasions blood transfusion had been required. She had also noticed small red spots appearing on her tongue, lips, face and fingers for the last fifteen years. Investigation of her family history revealed a total of eight relations, both ancestors and offspring, having similar conditions. Estimation of the bleeding time and the coagulation time gave normal results.

Dr. Isbister said that the patient was shown as she illustrated a rare disease; it was atypical, in that her symptoms had appeared later in life than usual.

Cyanosis.

DR. R. D. PUFLETT discussed the case of a male patient, aged thirty-three years, suffering from cyanosis. He had suffered from breathlessness for two years, from cough with sputum for two years, from cyanosis for one year and from hoarseness of the voice for one year. The patient said that his endurance had never been normal; he was unable to run or swim as far as his friends. Then in 1948 he had noticed "tightness" of the chest and breathlessness on walking up hills. At the same time a cough appeared which produced small amounts of thick white sputum. The breathlessness and cough progressed until slight exertion made him breathless, and coughing attacks were so severe that they were followed by "blackouts". In 1949 he became cyanosed, and that condition was associated with hoarseness of his voice. In 1937 the patient had undergone an operation for excision of a carcinoma of the lip and dissection of glands in the neck. The patient was a dealer; he was married and had one child; he smoked two ounces of tobacco per week and took alcohol occasionally. On examination of the patient, deep cyanosis, clubbing of the fingers, dyspnœa and wheezing were present. Dilated veins were seen in the neck. His pulse rate was 80 per minute. The blood pressure was 130 millimetres of mercury, systolic, and 100 millimetres, diastolic. The apex beat was not palpable; the heart sounds were normal. There was no œdema of the feet. The antero-posterior diameter of the chest was increased, and broncho-vesicular breath sounds were heard with occasional rhonchi at both lung bases. Examination of the vocal cords disclosed polypi, which were not causing obstruction. No other abnormalities were detected. During the patient's stay in hospital the cyanosis and breathlessness progressed and were not noticeably relieved by the administration of oxygen. Right-sided heart failure developed, and he died on June 9, 1950, seventeen days after his admission to hospital. While he was in hospital a number of investigations were carried out. An X-ray examination was made, and the radiologist gave the following report:

> Cardiac shadow not enlarged. Marked congestion of the pulmonary vessels, but bases show fine fibrosis with slight congestion, the result of a chronic inflammatory state. The pulmonary conus segment is slightly prominent. The ribs show old fractures. Barium swallow—normal.

An electrocardiogram was prepared, and the report was "right heart strain". A blood count gave the following information: the hæmoglobin value was 17·9 grammes per centum (119%), and the leucocytes numbered 13,600 per cubic millimetre, 80% being neutrophile cells, 1% eosinophile cells, 2% basophile cells, 12% lymphocytes and 5% monocytes. The Wassermann test produced a "doubtful positive" reaction. The vital capacity was 3·2 litres. Examination of a smear of the sputum revealed numerous well-preserved pus cells and occasional monilia organisms; culture revealed the presence of monilia. The diagnosis was considered to be (i) diffuse interstitial fibrosis of the lung, (ii) possibly Ayerza's syndrome.

Carcinoma of the Caecum and Diabetes Mellitus.

DR. H. HUNTER JAMIESON showed a female patient, aged sixty-two years, who had been admitted to hospital with a history of abdominal pain in the past two weeks. The pain was severe and generalized, associated with distension and occurring in two short-lived attacks. There was a ten years' history of *diabetes mellitus*. Partial obstruction was diagnosed and laparotomy revealed carcinoma of the caecum. The small bowel was anastomosed to the transverse colon and a transverse colostomy performed. Two weeks later the caecal growth was excised together with the right Fallopian tube and ovary, to which it was adherent. The growth was an anaplastic adenocarcinoma.

Carcinoma of the Rectum.

Dr. Jamieson's second patient, a woman, aged fifty-five years, had been admitted to hospital on November 20, 1945, with a twelve months' history of rectal bleeding with occasional attacks of abdominal distension. The result of X-ray examination after a barium enema was negative. Sigmoidoscopic examination revealed a mass at the recto-sigmoid junction, which biopsy showed to be carcinoma. The patient was severely anæmic. Hartmann's operation with left inguinal colostomy was performed and the patient was discharged from hospital well. One year later she was again admitted to hospital with a scanty blood-stained rectal discharge. Sigmoidoscopic examination revealed silk thread in the rectum. This was removed and bleeding ceased. In December, 1947, she was admitted to hospital with hæmaturia, and cystoscopic examination revealed a localized senile neoplasm of the left lateral wall of the bladder. This was coagulated and deep X-ray therapy was given. In January, 1949, cystoscopic examination revealed that the bladder wall was normal. In December, 1949, the patient was readmitted to hospital with colicky abdominal pain and occasional vomiting and abdominal distension. Cystoscopic examination again showed a normal bladder. The patient's condition settled down and she was discharged from hospital. On June 11, 1950, she was again admitted to hospital with a history of severe attacks of abdominal pain and vomiting for six weeks. X-ray examination showed small-bowel obstruction. Laparotomy was performed and the small bowel was found to be occluded by dense adhesions in the right iliac fossa. Ilium was anastomosed to ilium to by-pass the obstruction. No definite carcinoma was seen or felt at operation.

Acute Appendicitis in Hernial Sac.

Dr. Jamieson's last patient, a man, aged seventy-three years, had been admitted to hospital on December 9, 1949, complaining of severe pain in the right scrotal region of one day's duration; he had vomited several times before admission. He looked well, but was extremely tender to touch in the right iliac fossa, and over the external inguinal ring on the same side there was an irreducible right indirect inguinal hernia. At operation an acutely inflamed appendix was found in a right indirect hernial sac. The appendix was ligated and removed, the sac *plus* the right testicle and cord was excised, and the hernia was repaired. One week after operation the wound began to discharge. Then an infected hæmatoma containing a large amount of pus occurred in the right scrotal sac; this was opened and the discharge ceased.

Left Scrotal Swelling for Diagnosis.

DR. T. F. ROSE presented a man, aged thirty-eight years, who did not speak English. When first examined eight weeks before the meeting the patient had had a painful swollen left scrotal sac with a history of trauma two weeks earlier. The clinical findings were a hydrocele of the left testis and a swollen, tender, craggy swelling of the epididymis. X-ray examination of the chest revealed no abnormality, the result of a Mantoux test was positive, tests for syphilis yielded negative results, and no gonococci or significant pathogens were found from examination of a smear or culture of material obtained by prostatic massage. At the time of the meeting, after five weeks' observation, the swelling was much the same in size.[1] There was still some tenderness in the testis, epididymis and cord. The patient appeared to have right-sided sciatica and pain in the right shoulder.

Cancellous Iliac Graft for Non-Union of Fracture.

Dr. Rose then presented a young man whom he had treated in conjunction with Dr. Basil Riley. The patient had incurred a compound fracture of the shaft of the right tibia and fibula in June, 1947, as a result of a motor cycle accident; there was much comminution of the bones and soft tissue damage, with loss of skin over the fracture site. The wound was excised, and the fragments were wired together. Skin was mobilized to cover the fracture site. The raw area left was later grafted with a partial-thickness skin graft. A large piece of bone forming the whole thickness of the tibial shaft then sequestrated and caused a sinus. The bone was removed, as also were the pieces of wire. It was obvious that non-union would occur owing to the loss of bone from the tibia after the sequestrum was removed, so it was decided to insert a bone graft. To make sure that that would succeed, it was decided to replace the split skin graft by a full-thickness pedicle graft from the abdomen. That was done by Dr. Basil Riley in stages from September 9, 1948, to February 16, 1949. The graft took well, and on March 23, 1949, the fracture site was exposed by raising one edge of the graft. The fibrous tissue between the fracture ends was excised, the free ends of the bones were freshened, and cancellous chips were removed from the ilium and inserted into the gap between the bone ends. The wounds healed well. By September 22, 1949, the patient was walking on a caliper and on March 1, 1950, the X-ray appearance showed good consolidation of the graft. Clinically, too, there was firm union. Dr. Rose pointed out that all operative manœuvres had been performed under penicillin cover.

Pharyngeal Diverticulum.

Dr. Rose also presented a patient who had been treated for a pharyngeal diverticulum. This patient will be the subject of a detailed case report to be published at a later date.

Thyreotoxicosis Plus Confusional State.

DR. F. F. RUNDLE presented a woman, aged forty-five years, who in November, 1949, had been admitted to hospital and found to have a large nodular goitre and symptoms and signs of mild thyreotoxicosis. She was also complaining of vague abdominal pain, and while that was being investigated subsequently, with the patient as an out-patient, she developed a confusional state, for which she was readmitted to hospital. She was given shock therapy and made a good recovery from her confusional state, being discharged from hospital after six weeks' in-patient treatment. During her convalescence the cause of severe psychic trauma related to her marital state was unearthed, and her difficulties in this connexion were straightened out. For the subsequent period she had been treated with methyl thiouracil, 50 milligrammes daily, and at the time of the meeting was clinically in a euthyreoid state. Her weight had increased slightly, from eight stone four pounds to nine stone in the past fortnight. Dr. Rundle commented that the patient was shown as representing the combination of thyreotoxicosis and severe psychiatric disorder. The thyreotoxicosis was judged to be a minor factor in her total clinical state. Further the psychic trauma associated with an operation would be great in her case. Therefore medical management had been advised.

Severe Thyreotoxicosis.

Dr. Rundle then presented a woman, aged twenty-four years, who had developed symptoms of thyreotoxicosis shortly after the birth of her second child. The first child had died during the pregnancy, and the patient had also lost her father shortly before. She attended the medical department of a big metropolitan hospital and responded well to treatment with methyl thiouracil. When she again became pregnant and was transferred to the obstetric department, antithyreoid therapy seemed to have lapsed, though she remained fairly well during the pregnancy. After her confinement she was so occupied with the household and her children that she stopped attending hospital altogether. Finally, in January, 1950, nearly three years after its first onset, she had come again to hospital for treatment with fully developed Graves's disease. She was shaky, irritable and easily tired, and had lost one stone in the six weeks prior to attending hospital. On physical examination she presented all the signs of severe thyreotoxicosis: a diffuse pulsatile goitre, tachycardia (120 per minute), tremor, muscular wasting, and hyperexcitability. After preparation with methyl thiouracil and iodine, bilateral subtotal thyreoidectomy was performed. At the time of the meeting the patient was symptom free and duly grateful for having completed her treatment.

Ophthalmic Type of Graves's Disease.

Dr. Rundle's next patient, a man, aged forty-four years, had first attended hospital in November, 1949, when he stated that his eyes had been noticeably prominent for four to five months; he had other symptoms suggestive of thyreotoxicosis, including recent irritability, bulimia, loss of weight and fatigability. Examination of the patient showed much retraction of both upper lids with probable bilateral exophthalmos. The exophthalmometer reading in the right eye was 14·5 millimetres and in the left eye 13·5 millimetres. There was moderate limitation of elevation of the left eye. The thyreoid gland was not palpable, and the pulse rate was 66 per minute. The basal metabolic rate was *plus* 37%. In view of the symptoms and raised metabolic rate, the patient was given methyl thiouracil 50 milligrammes twice a day. That had since been reduced to 50 milligrammes daily. Dr. Rundle said that since coming under treatment the patient had gained nearly two stone in weight and had lost his general symptoms. The thyreoid gland was still not palpable. The ocular manifestations were virtually unchanged.

Carcinoma Recti with Invasion of Cervix and Vagina.

Dr. Rundle next presented a woman, aged forty-nine years, who had suffered from intermittent attacks of diarrhœa, the passage of excessive flatus *per rectum*, anorexia, and steady loss of weight for twelve months. In the attacks she was called to stool up to sixteen times in the twenty-four hours, but passed only small amounts of blood and mucus. The first attack persisted for four months, but was "relieved by wash-outs and olive oil enemata". She had lost one stone in weight. Examination of the patient revealed that her general condition was good. There was no evidence of abdominal or other metastases. Pelvic examination revealed a large ulcerating mass high in the rectum, extending round its whole circumference and fixed to the cervix anteriorly. Through a lower mid-line abdominal incision the abdomen was explored. The liver and peritoneum generally were healthy. The large recto-cervical mass was slightly movable. The superior hæmorrhoidal glands were enlarged to the level of the pelvic brim. Wertheim's operation was performed *plus* abdomino-perineal excision of the rectum. The patient was ambulatory six days afterwards and was discharged from hospital after six weeks, the perineal wound being somewhat slow to heal. The mass was found on examination to be an adenocarcinoma of the rectum. The whole circumference of the rectum was involved for a length of five centimetres, the bowel wall being penetrated in several places. The local lymph glands were involved, and microscopic spread to the vagina was demonstrated in one of the sections.

Œsophageal Hiatus Hernia with Penetrating Œsophageal Ulcer.

Dr. Rundle's next patient, a man, aged fifty-two years, had been first admitted to Prince Henry Hospital in June, 1948, with hæmatemesis and melæna. He had had epigastric and substernal pain after meals for eighteen months. X-ray examination after a barium meal showed a hiatus hernia with probable œsophageal ulceration. His general condition was satisfactory, and a trial of palliative treatment was recommended. But after he left hospital his attacks of pain worsened, and he would vomit all foods for two weeks at a time. In December, 1949, he was readmitted to hospital because of further hæmatemesis and loss of weight. His general condition was satisfactory, and there was no

[1] Operation performed a week later revealed the swelling to be an organized hæmatoma in a spermatocele.

evidence of systemic disease apart from secondary anæmia. The hæmoglobin percentage was 62, but increased to 95 with a pre-operative blood transfusion. At operation on January 12, 1950, through a left thoraco-abdominal incision, a large œsophageal hiatus hernia was found, rather more than half the stomach being in the posterior part of the mediastinum. The diphragm was divided back to the œsophageal hiatus. The cardia and fundus of the stomach and the lower part of the œsophagus were mobilized from the surrounding structures and drawn downwards. It was then found possible to reconstitute a closely fitting œsophageal hiatus by repairing the diaphragm anteriorly and laterally, the œsophagus being displaced to the medial end of the former hiatus. In the mobilization of the lower part of the œsophagus its lumen was entered through the wall of a long-standing, penetrating ulcer. Fatty and fibrous infiltration rendered identification of the œsophageal wall difficult. The ulcer was closed with interrupted sutures of fine silk. The remainder of the diaphragm was then repaired and the wound closed with drainage down to the operation site. Recent X-ray examination showed the passage of a bolus to be normal and the cardia and fundus of the stomach to be well down in the abdomen. The patient was symptom free and in fact stated that he felt better than for years past.

Large Diverticulum of Cardia of Stomach.

Dr. Rundle then presented a man, aged forty-nine years, who had suffered from upper abdominal pain occurring on and off for six years and becoming much worse during the past year. The pain would spread to both hypochondriac zones and occasionally towards the left iliac fossa. It was worse when he lay on his right side. During the past year his appetite had failed, and he had vomited repeatedly. He had vomited blood on two occasions, once profusely. Examination of the patient showed no abnormal physical signs apart from pallor and slight epigastric tenderness. X-ray examination after a barium meal revealed a large diverticulum of the cardiac region of the stomach. At operation on May 11, 1950, invagination of the diverticulum was carried out. The diverticulum was found on the posterior aspect of the stomach, near the lesser curvature just below and medial to the cardiac orifice. It was thin-walled, cylindrical and readily distensible, being about one and a half inches in diameter and of equal depth. Its junction with the stomach was not constricted. But the fundus of the diverticulum was embedded in the upper border of the pancreas. Its wall was friable and appeared to be infected. The whole diverticulum was invaginated with two layers of interrupted sutures of fine silk.

Œsophageal Hiatus Hernia.

Dr. Rundle's last patient, a man, aged forty-six years, had had a history of two to three years' postprandial discomfort, retrosternal pain and eructations, steadily becoming worse, as well as nausea and vomiting on occasions. All the symptoms were greatly aggravated when the patient was in the recumbent posture. He was frequently wakened by "indigestion" at night and then became comfortable only when he propped himself up. X-ray examination after a barium meal showed a pronounced herniation of the fundus of the stomach into the mediastinum. At operation on April 21, 1950, through a left thoraco-abdominal incision, the presence of a hiatus hernia was verified. The hiatus was repaired, after its edges had been defined and the stomach had been drawn down into the abdomen. Interrupted sutures of thick silk were used. The patient's symptoms had been relieved and recent X-ray examination had shown the passage of a barium bolus to be normal and the stomach to be wholly intraabdominal.

Silent Carcinoma of the Kidney.

DR. ALBAN GEE showed a patient with carcinoma of the kidney which had presented no symptoms, but the presence of which had been indicated by pathological examination of a mass removed from the chest wall. The patient, a man, aged fifty-one years, had presented himself to Dr. A. Foldes, having noticed dilated veins running across the right side of the chest. Dr. Foldes found a supraclavicular tumour, which on fluoroscopic examination was seen to extend below the clavicle also. The patient was then referred to Dr. M. P. Susman, who removed a mass measuring five inches by four inches by three inches from the vault of the right side of the thorax, where it had replaced most of the first rib. The lung was not involved. A pathological report by Dr. K. Viner Smith indicated that the tissues consisted of fairly large cells with very lightly staining cytoplasm in small groups, separated by a little fibrous tissue, and that it appeared to be a metastatic growth from a carcinoma. The microscopic picture was suggested of a Grawitz's tumour of the kidney. An excretion urogram showed a normal collecting system on the right side, but on the left side there was a small bulge in the renal outline towards the lower pole. There was irregularity and clubbing of the middle and lowest calyces, and the inferior infundibulum was elongated and thinned out. The middle infundibulum was not seen. Bilateral retrograde pyelograms confirmed these findings, both infundibula giving the impression of having a mass in between them which was exerting pressure on both. An indigo-carmine test gave a blue result from each side, but it was considerably less intense from the left. Presence of a tumour of the lower pole of the left kidney was postulated, and that was confirmed at subsequent nephrectomy. A pathological report by Dr. C. S. Graham indicated that it was a typical renal carcinoma of the large clear-cell type, the type and growth pattern being the same as those of the tumour previously removed from the first rib.

Dr. Gee remarked that the interest of the case discussed lay in the completely silent nature of the primary growth. At no stage could any symptoms or signs be referred to the urinary system. The patient had not lost weight, and generally felt very well, carrying on his occupation of a poultry farmer. Often renal cortical tumours were found only by chance on abdominal palpation when they had reached a large size. Hæmaturia and pain were frequently absent, in contradistinction to renal pelvic tumours, which bled fairly easily. An excretion urogram should always be taken in doubtful cases.

Foreign Body in Bladder.

Dr. Gee's next patient was a girl, aged four years, who, while holidaying in the country, had inserted a bobby pin (large size) into her bladder. It had caused some distress, particularly at the end of micturition, when blood was passed. She had been examined rectally and vaginally with negative result, after an X-ray examination had shown the pin lying transversely in the bony pelvis. On cystoscopic examination the pin could be seen lying across the trigone and was removed by hooking a stylet wire into its curved end.

Dr. Gee commented that foreign bodies of any length in the bladder usually lay in the transverse axis. He said that when the patient was questioned as to why she had inserted the pin, she stated that she had been "itchy" there. That had led to the subsequent finding of a heavy threadworm infestation—a not uncommon cause of urinary symptoms.

Urinary Calculi Complicating Pregnancy.

Dr. Gee next presented two women patients who had stone in the urinary tract and were also pregnant. The first patient was aged thirty-seven years and four months pregnant. She had three children, aged eighteen, seventeen and nine years respectively, and apart from a raised blood pressure and left loin pain during the last confinement, had been free from complications. Her presenting symptom was pain in the left loin, which had been present ever since the birth of her youngest child. The pain was fairly constant in character, but there were occasions of acute exacerbation during which it radiated to the left inguinal region. Frequency and scalding were associated with micturition, but never hæmaturia. Her blood pressure was 150 millimetres of mercury (systolic) and 100 millimetres (diastolic). She was tender over her left kidney, but no other abnormality was detected. Microscopic examination of the urine revealed eight to ten pus cells per high-power field, but it was found to be sterile. An excretion urogram showed a mulberry calculus in the left renal pelvis with considerable calyceal dilatation. A left pyelolithotomy was performed, and the patient was discharged from hospital a fortnight later. Her pregnancy continued uneventfully.

In discussing the patient, Dr. Gee said that stone was not of common occurrence during pregnancy, most figures placing the incidence at about once in every two thousand deliveries. A stone obstructing the urinary tract was always of major importance, and as pregnancy advanced, the possibility of superimposed infection was increased. Pyonephrosis was then apt to develop, often without local symptoms, and the destruction of renal tissue was greatly accelerated. The ideal time to remove such stones was during the fourth month, when the technical procedures from both the mechanical and the vascular points of view were infinitely easier. In general, it might be said that all except small calculi should be removed during the first four months of pregnancy, particularly in the presence of infection.

Dr. Gee's last patient was a woman, aged thirty years, who had been admitted to hospital suffering from lower abdominal pain. It was present constantly in the form of an ache when she was lying or sitting, and was accentuated when she walked or after she passed urine. When micturating, she had to bend forward or there would be an obstruction to the flow, and at the conclusion she again had the desire to pass urine. Blood had been passed on several occasions. There was a past history of recurrent attacks of pyelonephritis and cystitis since the age of fifteen years, and she had lost two and a half stone in weight in the previous eighteen months. Her blood pressure was 144 millimetres of mercury (systolic) and 88 millimetres (diastolic). Her last normal menstrual period had been two and a half months previously, and she had other signs of pregnancy. She had three children, aged eight, six and three years respectively, and some degree of toxæmia had been present during each pregnancy. She looked ill, lying listlessly in bed, and had noticeable tenderness in the hypogastrium and both renal angles. The gynæcologist was unable to map out the size of the uterus owing to non-cooperation and tenderness, but felt a hard area in the bladder position. Her urine contained numerous pus cells per high-power field, and a heavy growth of coliform organisms was obtained on culture. Albumin was present. A plain X-ray picture revealed a dense shadow in the bladder area as big as a medium-sized egg. The patient appeared to have an acute urinary infection involving both upper tracts as well as the bladder, and an indwelling catheter was inserted. Sulphonamides were given and, although pus cells persisted in the urine, there was later no growth on attempted culture. After a week's drainage of the bladder, she was much improved; in an indigo-carmine test a fifteen-minute delay occurred before blue was seen, but the concentration was satisfactory. An excretion urogram showed normal upper urinary tracts and localized the opacity to the bladder. After a fortnight, a suprapubic cystotomy was performed and the stone removed. The wound was closed as after a Harris prostatectomy, and was healed one week after operation, urine being then passed normally.

Dr. Gee remarked that stone in the female bladder was an uncommon condition, particularly of the size found in the last patient presented, and that it was a rare finding in pregnancy. He said that Crabtree had stated that none were seen in over twenty years at the Boston Lying-in Hospital, and other authors described it as similarly uncommon. Its importance lay in the facts that it was always a nidus for infection, and could cause pressure necrosis on the bladder wall during labour. At the time of the meeting the patient presented was eight months pregnant, and was carrying on without further complications.

(To be continued.)

AUSTRALIAN ASSOCIATION OF PHYSICAL MEDICINE (BRITISH MEDICAL ASSOCIATION).

A MEETING of the Australian Association of Physical Medicine (British Medical Association) will be held in Sydney from October 23 to 25, 1950. The programme is as follows.

Monday, October 23: 2.30 p.m., at the Stawell Hall, 143 Macquarie Street, Sydney, "Ankylosing Spondylitis", Dr. L. J. A. Parr (medical aspects), Dr. B. G. Wade (physiotherapy); 8 p.m., at British Medical Association House, 135 Macquarie Street, Sydney, "Ankylosing Spondylitis", Dr. E. Frecker (radiological diagnosis and therapy).

Tuesday, October 24: 2 p.m., clinical meeting at Royal Prince Alfred Hospital, Camperdown, Dr. S. Nelson and Dr. B. G. Wade; 8 p.m., at British Medical Association House, "Osteoarthritis of the Hip Joint", Dr. S. Scougall (surgical aspect), Dr. F. May (physiotherapy).

Wednesday, October 25: 2 p.m., clinical meeting at Balmain District Hospital, Dr. L. J. A. Parr; 8 p.m., at British Medical Association House, annual meeting and presidential address.

Thursday, October 26: 9.30 a.m., clinical meeting at Royal South Sydney Hospital, Dr. L. J. A. Parr.

Correspondence.

ACUTE MYOCARDITIS.

SIR: We are indeed grateful to Dr. Bowden for drawing attention to the frequency of myocarditis as a cause of sudden death. Except in diphtheria and the rheumatic diseases, we are not accustomed to paying more than perfunctory attention to the functional state of the myocardium in infective diseases; clearly we ought to be more meticulous, for Dr. Bowden's observations lead us to suppose that histo-pathological changes in heart muscle in poliomyelitis and other viral and bacterial infections are commoner than one supposes, and have, naturally, an important prognostic significance. Close attention to electrocardiographic studies should provide in life an estimate of the frequency of these changes.

Regarding Dr. Bowden's sixth case, one is not happy, in reading the protocol, that an unqualified pathological diagnosis of "acute myocarditis" explains the bizarre clinical picture described. It is unfortunate that so many important investigations are not recorded. The picture described is of a young women with a severe pyrexial illness having a fatal outcome, with evidence of at least involvement of the visceral organs, the heart, and the peripheral nervous system. A clinical diagnosis of *periarteritis nodosa* is at once suggested. Certain of the clinical features of Dr. Bowden's case point to extensive renal involvement—the hypertension, and the uræmic symptoms; but there is no account given of renal involvement studied in life or at autopsy. Pain referable to the visceral organs, hypertension and hæmaturia, and polyneuritis are all well-known manifestations of *periarteritis nodosa* (Miller and Daley, 1946), and where the pathological changes are widespread in the body, it is more than likely that the atrerioles of the coronary circulation will be affected, causing precisely those changes in the myocardium that Dr. Bowden described. At autopsy in this case "many subpleural hæmorrhages" were described; were these examined microscopically, and is it not possible that a close histo-pathological examination of the small arterioles at various sites, in particular in the kidney, might have revealed the characteristic changes in the walls typical of *periarteritis nodosa*?

Yours, etc.,

ERIC G. SAINT, M.D., M.R.A.C.P., B.Sc.

Port Hedland,
Western Australia,
September 30, 1950.

Reference.

Miller, H. G., and Daley, R. (1946), "Clinical Aspects of Polyarteritis Nodosa", *The Quarterly Journal of Medicine*, Volume XV, page 255.

THE PHARMACEUTICAL BENEFITS ACT AND DRUGS IN SHORT SUPPLY.

SIR: The widespread prescribing by the profession of certain drugs and preparations included in the list of life-saving and essential drugs issued under the *Pharmaceutical Benefits Act* has brought about shortages in certain items which, if not watched carefully by the prescribing doctor, may lead to the complete failure of supply.

Some of the items are in short supply throughout the world, whilst others are only obtainable from dollar sources. Apart from certain biological products, vaccines and sera which are completely prepared in Australia, many of the drugs which are packed or even manufactured in Australia depend for some stage of their preparation on imported materials. In view of the international situation it is particularly desirable that Australia should ensure that adequate supplies of essential drugs are held in reserve.

A committee has been established to study the problem and to make recommendations to meet it.

Under the regulations of the *Pharmaceutical Benefits Act* four benefits—namely, aureomycin, chloramphenicol, streptomycin and dihydrostreptomycin—have been listed as not being available as a free issue unless the doctor writes on the prescription form: "I certify that in my opinion there is no other drug which would be equally effective in this case."

Whilst the profession has complied with this condition, the demand for these benefits exceeds the available supply and other means for their distribution may have to be considered.

The profession is earnestly requested not to prescribe these benefits whilst the present shortage exists unless they are convinced that no other drug would be of any value.

The action of antibiotics is usually limited to specific organisms, and unless the organism is known the use of the antibiotics may well be unjustified. In certain diseases

"sulpha" drugs or penicillin will be found to supply the needs of the patient, and it is thought that their use should be tried before ordering benefits which are in short supply.

If this is not conscientiously done by the whole of the profession it is inevitable that some patients in urgent need of this form of treatment will be deprived of the drugs with the risk of unfortunate consequences.

Yours, etc.,

A. J. METCALFE,
Director-General of Health.

Commonwealth of Australia,
Department of Health,
Canberra, A.C.T.
October 6, 1950.

Obituary.

PAUL GREIG DANE.

WE regret to announce the death of Dr. Paul Greig Dane, which occurred on October 6, 1950, at Melbourne.

Royal Australasian College of Surgeons.

OPEN MEETING.

A SPECIAL MEETING of the Royal Australasian College of Surgeons will be held on Wednesday, October 25, 1950, in the Stawell Hall of The Royal Australasian College of Physicians, 145 Macquarie Street, Sydney, at 8.15 p.m. The subject will be "Surgery of Peripheral Vascular Disease", and the speakers will be Dr. I. D. Miller and Dr. J. Fleming. This meeting is open to all members of the medical profession.

Notice.

THE Victorian State Committee of the Royal College of Obstetricians and Gynæcologists is anxious to establish a library and museum of old books and instruments of obstetrical and gynæcological interest. They would be grateful for gifts from the cupboards and shelves of members of the medical profession. Further information may be obtained from the headquarters of the committee, 122 Flinders Street, Melbourne, C.1.

Australian Medical Board Proceedings.

TASMANIA.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Act*, 1918, of Tasmania, as duly qualified medical practitioners:

Batt, Eric Harrison, M.B., Ch.B., 1946 (Univ. Leeds), Launceston, Tasmania.

Batt, Betty Joan, M.R.C.S. (England), L.R.C.P. (London), M.B., B.Ch. (Cantab.), 1948, Launceston, Tasmania.

Felstead, James Ballard, M.B., B.S., 1942 (Univ. Melbourne), Launceston, Tasmania.

Hendrie, Agnes Lees, M.B., Ch.B., 1922 (Univ. Glasgow), Bothwell.

Hendrie, Matthew Lapsley, L.R.C.S., L.R.C.P. (Edinburgh), 1925, L.R.F.P.S. (Glasgow), 1925, Bothwell.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED SEPTEMBER 30, 1950.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.[2]	Australia.
Ankylostomiasis	*	..	..	..	..	..	..	..	..
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	4(4)	2(2)	..	..	..	..	..	..	6
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(a)	*	*	..	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	..	..	..	..	..	..	..
Diphtheria	9(5)	5(5)	8(4)	2(2)	3(2)	1(1)	..	..	28
Dysentery (Amœbic)	*	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	*	..	5(4)	..	1	..	..	..	6
Encephalitis Lethargica	..	..	..	..	1	..	..	..	1
Erysipelas	*	*	*	1	*	*	..	..	1
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	..	*	*	..	*	*	..	..
Influenza	*	*	*	..	*	*	..	*	..
Lead Poisoning	*	*	..	*	*	*	*	*	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(b)	*	..	1	..	..	..	..	..	1
Measles	*	*	*	275(203)	*	*	..	..	275
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	10(5)	..	..	8(7)	2(2)	..	..	..	20
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella(c)	*	*	..	*	2(2)	1(1)	..	..	3
Scarlet Fever	14(11)	13(8)	7(4)	11(6)	4(2)	4(1)	..	..	53
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	..	*	*	*	*	*	..
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(d)	23(21)	20(11)	4(1)	7(7)	8(7)	5(2)	..	..	67
Typhoid Fever(e)	1(1)	..	..	..	..	..	..	..	1
Typhus (Endemic)(f)	..	..	..	..	1(1)	..	..	..	1
Undulant Fever	..	1	..	..	..	..	..	..	1
Weil's Disease(g)	*	*	7	*	*	*	*	*	7
Whooping Cough	*	*	*	3(3)	*	*	..	..	3
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946–1947. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from the Northern Territory and Australian Capital Territory.
* Not notifiable.
(a) Includes Mossman and Sarina fevers. (b) Mainly relapses among servicemen infected overseas. (c) Notifiable disease in Queensland in females aged over fourteen years. (d) Includes all forms. (e) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (f) Includes scrub, murine and tick typhus. (g) Includes leptospiroses. Weil's and para-Weil's disease.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 59, of October 5, 1950.

CITIZEN NAVAL FORCES OF THE COMMONWEALTH.

Royal Australian Naval Volunteer Reserve.

Promotion.—Surgeon Lieutenant John Joseph Herlihy is promoted to the rank of Surgeon Lieutenant-Commander, dated 21st July, 1950.

AUSTRALIAN MILITARY FORCES.

Citizen Military Forces.

Northern Command: First Military District.

Royal Australian Army Medical Corps (Medical): To be Captain (provisionally), 15th August, 1950.—1/13388 Charles George Drury Clarke.

Southern Command: Third Military District.

Royal Australian Army Medical Corps (Medical): To be Captains (provisionally), 7th August, 1950.—3/101015 John Liddell Stubbe, 3/101812 Peter John Ryan and 3/101014 John MacKinnon Grant.

Tasmanian Command: Sixth Military District.

Royal Australian Army Medical Corps (Medical): To be Temporary Colonel, 16th August, 1950.—6/15311 Lieutenant-Colonel (provisionally) P. Braithwaite.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps.

1st Military District.—To be Honorary Captain, 15th August, 1950: Mark Robin Harrison. To be Honorary Captain, 31st July, 1950: Peter Francis Gill.

2nd Military District.—The name appearing in Executive Minute No. 134 of 1950, promulgated in *Commonwealth Gazette* No. 38 of 1950 as N. D. Dunbar, is amended to read N. D. Barton.

3rd Military District.—Lieutenant-Colonel W. S. J. P. Heslop, E.D., is placed upon the Retired List (3rd Military District) with the honorary rank of Colonel and with permission to wear the prescribed uniform, 7th August, 1950. The following officers are placed upon the Retired List (3rd Military District) with permission to retain their rank and wear the prescribed uniform, 7th August, 1950: Captain (Honorary Major) H. F. Praagst and Captain F. L. Nance. To be Honorary Captain, 29th May, 1950: Lieutenant C. H. M. Haydon.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force: Medical Branch.

The probationary appointment of Flight Lieutenant J. N. Diggle (033066) is confirmed.

Active Citizen Force: Medical Branch.

The appointment of Temporary Squadron Leader G. M. Colditz (021961) is terminated on demobilization, 27th May, 1950.

Flight Lieutenant W. R. Pitney (257530) (part time) is transferred to the Reserve, 10th June, 1950.

Flight Lieutenant G. A. Robbie (256865) is transferred from the Reserve, 12th June, 1950, for part-time duties.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Keating, Bruce Ivor, M.B., B.S., 1950 (Univ. Sydney), 27 Stanley Avenue, Mosman.

Hennessy, William Bertram, M.B., B.S., 1950 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

Kyneur, Frederick James, M.B., B.S., 1950 (Univ. Sydney), Saint Joseph's Hospital, Auburn.

The undermentioned has applied for election as a member of the Victorian Branch of the British Medical Association:

James, Paul Reuben, M.B., B.S., 1941 (Univ. Adelaide), 42 Fitzroy Street, St. Kilda.

The undermentioned have been elected members of the South Australian Branch of the British Medical Association:

Linn, John Graham, M.B., B.S., 1950 (Univ. Adelaide), Royal Adelaide Hospital, Adelaide.

Harbison, John Henry, M.B., B.S., 1949 (Univ. Adelaide), Royal Adelaide Hospital, Adelaide.

Topliss, John George, M.B., B.S., 1950 (Univ. Adelaide), 18 Ranelagh Street, Woodville, South Australia.

Medical Appointments.

Dr. Lawrence William Alderman has been appointed a member of the State Children's Council of the Northern Territory.

Diary for the Month.

OCT. 24.—New South Wales Branch, B.M.A.: Ethics Committee.
OCT. 25.—Victorian Branch, B.M.A.: Council Meeting.
OCT. 26.—New South Wales Branch, B.M.A.: Branch Meeting.
OCT. 26.—South Australian Branch, B.M.A.: Clinical Meeting.
OCT. 27.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney)—All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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